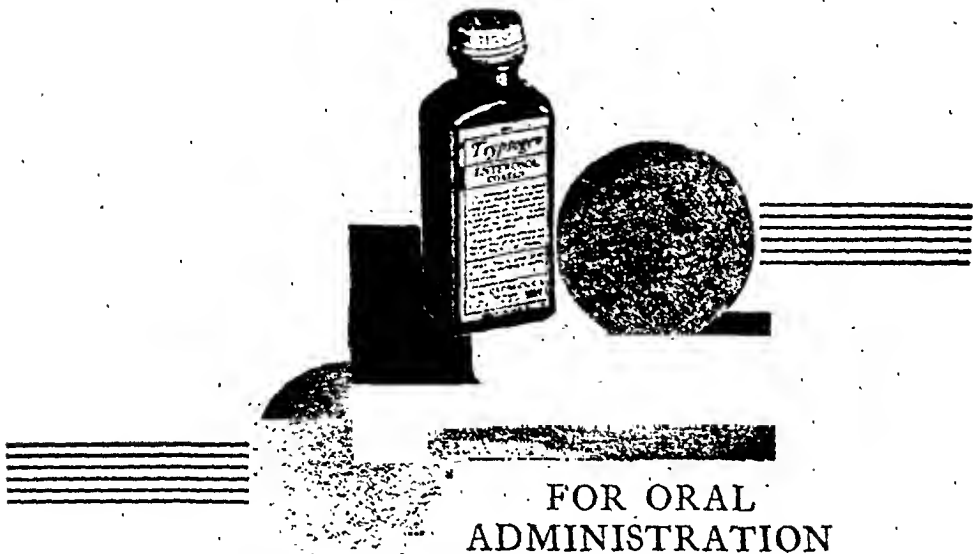


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Contents

	Page		Page
Acute Anterior Poliomyelitis. <i>H. H. Hyland, W. J. Gardiner, F. C. Heal, W. A. Oille and O. M. Solandt</i> . . .	1	Two Cases of Bilateral Spontaneous Pneumothorax. <i>D. B. Westcott</i> . . .	57
Experimental Studies with Sulphanilamide and Other Compounds. <i>P. H. Greco</i> . . .	12	Papillary Squamous-cell Epithelioma of the Renal Pelvis. <i>A. Strasberg</i> . . .	58
The Use of Sulphanilamide in Clinical Medicine. <i>W. H. Brown</i> . . .	15		
A Preliminary Report on Sulphanilamide as a Urinary Antiseptic. <i>D. R. Mitchell</i> . . .	22	CASE REPORTS	
Silicosis: An Experimental Study of the Leaching of Silicates in Tissues. <i>H. E. Williams and D. A. Irwin</i> . . .	26	A Case of Unusual Calcium Deposition Due to Raynaud's Disease. <i>C. J. Houston and E. Johnson</i> . . .	60
A Hypoglycæmic Substance from the Roots of the Devil's Club (<i>Fatsia Horrida</i>). <i>R. G. Large and H. N. Brocklesby</i> . . .	32	An Unusual Head Injury. <i>C. K. Fuller</i> . . .	61
Present Day Problems in the Management of Diabetes. <i>F. N. Allan</i> . . .	36	Congenital Rhabdomyoma of the Heart. <i>M. V. Rae</i> . . .	63
Allergy in Childhood. <i>H. L. Bacal</i> . . .	41		
Modern Trends in Child Psychiatry. <i>C. H. Gundry</i> . . .	46	THERAPEUTICS AND PHARMACOLOGY	
Some Observations on Petrous Tip Suppuration. <i>D. E. S. Wishart</i> . . .	50	Sulphanilamide in Genito-urinary Infections. <i>N. E. Berry</i> . . .	65
		The Management of the Premature Infant. <i>H. McGarry</i> . . .	66
		EDITORIALS	
		The Etiology of Appendicitis . . .	67
		The Regulation of Blood Transfusion . . .	69

CONTINUED ON PAGE IV

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CONTENTS CONTINUED FROM PAGE II

	Page		
EDITORIAL COMMENTS		LETTERS, NOTES AND QUERIES	
Medical Students Form an Organization	70	Post Hoc Ergo Propter Hoc Fallacy	
International Academy for Post-graduate Medical Work	70	The Care of the Hypodermic Syringe	
RETROSPECT		Sterilization of Hypodermic Syringes	
European Trends in Irradiation Therapy. <i>E. Trapp</i>	71	Poison Ivy	
SPECIAL ARTICLE		TOPICS OF CURRENT INTEREST	
Diet and Nutrition		Poliomyelitis Infectivity of Human Stools	
Nutritional Requirements of the Mother During Lactation. <i>I. M. Rabinowitch</i>	76	Interference with Wireless Reception by Electro-medical Apparatus	
MEDICAL ECONOMICS		Air-conditioning	
Medical Economics. <i>J. A. Hannah</i>	79	ABSTRACT FROM CURRENT LITERATURE	
HOSPITAL SERVICE DEPARTMENT NOTES		Medicine	
Educational Films	81	Surgery	
MEDICAL SOCIETIES		Obstetrics and Gynecology	
Montreal Medico-Chirurgical	81	Urology	
Montreal Physiological	82	Neurology and Psychiatry	9
Saint John	85	Therapeutics	9
St. Joseph's Hospital, Winnipeg	85	Pathology and Experimental Medicine	
Saskatoon and District	85	Hygiene and Public Health	
Winnipeg	85	OBITUARIES	
POST-GRADUATE COURSES		W. A. Anderson	96
Edinburgh University	85	E. D. Aylen	96
New York Academy of Medicine	85	J. L. Biggar	96
UNIVERSITY NOTES		O. W. Bradley	97
Dalhousie	86	H. H. Galloway	97
Manitoba	86	G. L. Hume	97
McGill	86	R. J. Ledwell	97
Toronto	87	F. D. Llorens	97
Western Ontario	87	J. Moore	97
		A. W. Richardson	97
		H. Ross	97
		J. G. Toombs	97
		J. F. Wood	98
		NEWS ITEMS	
		Canada	98
		United States	102
		General	102
		Book Reviews	104

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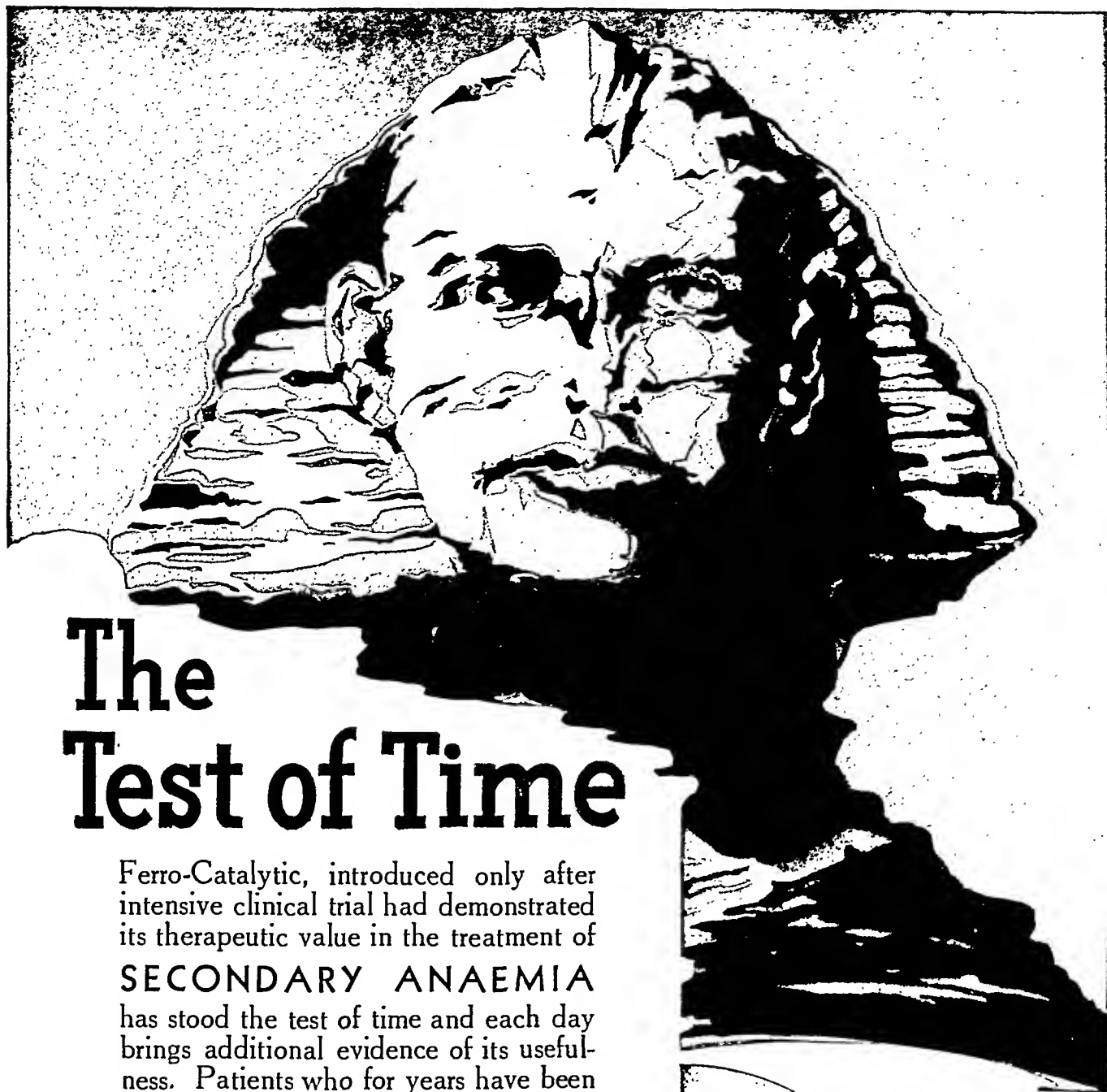
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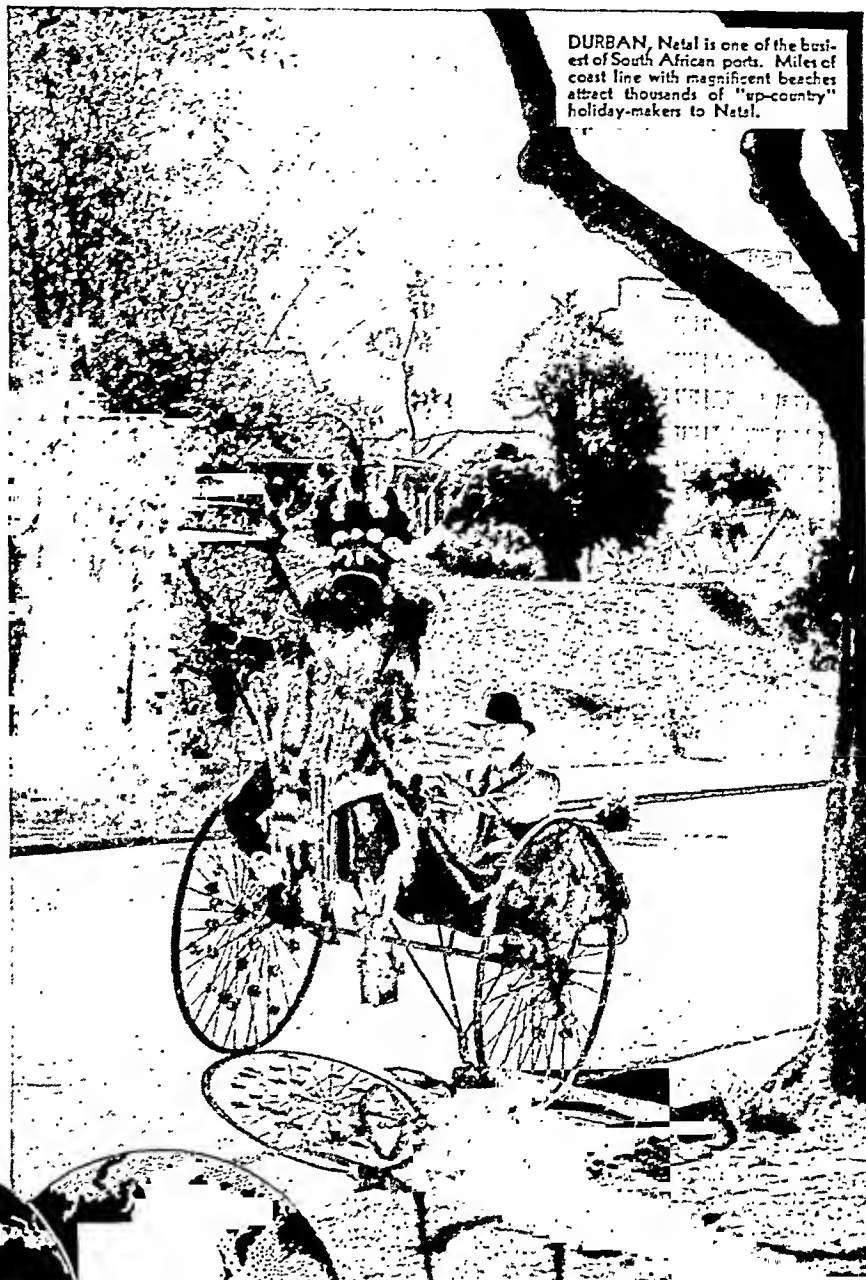
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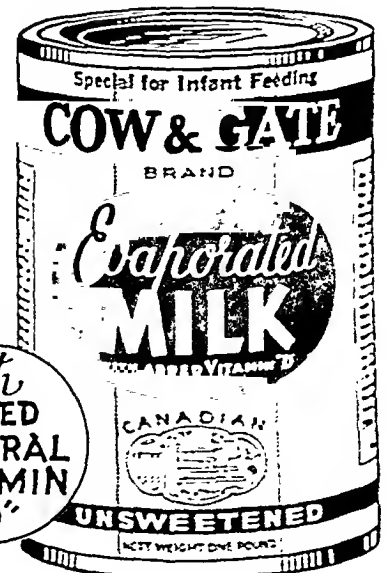
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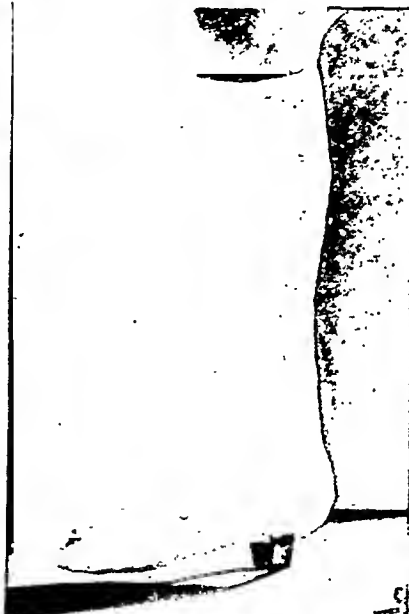
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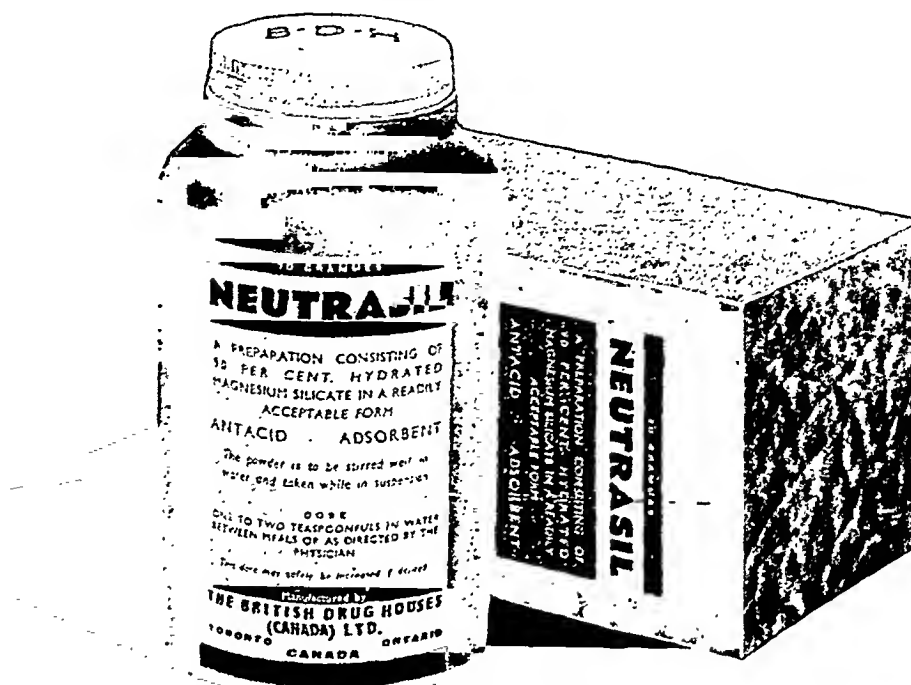
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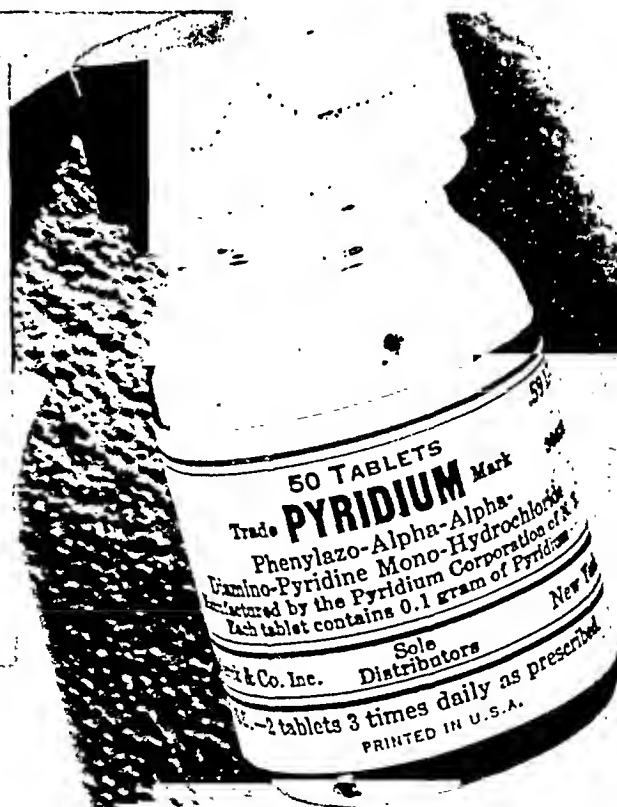


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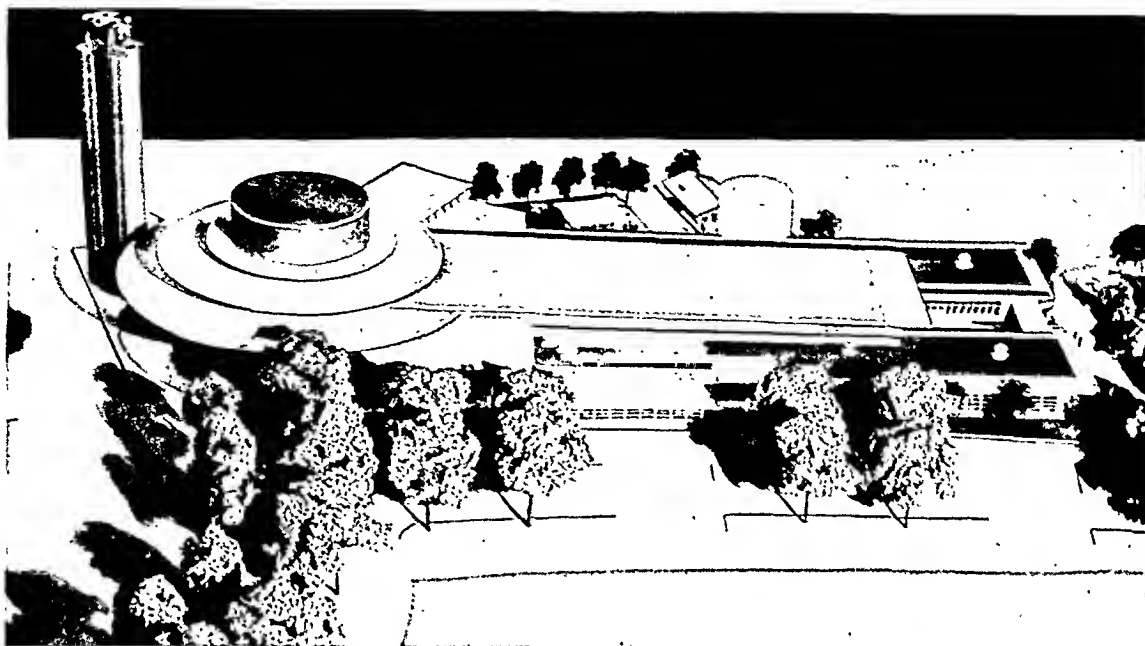
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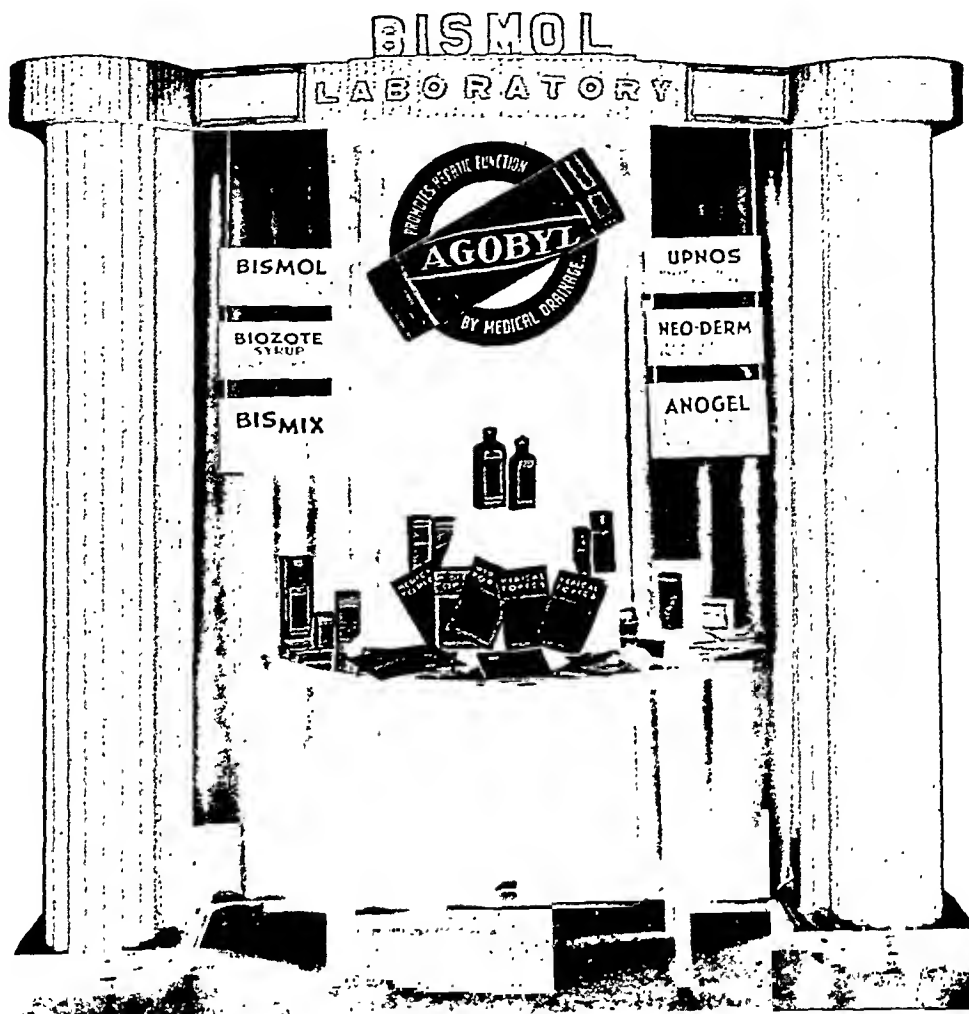
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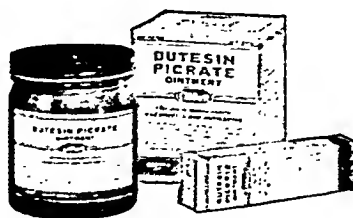
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No. 1

ACUTE ANTERIOR POLIOMYELITIS*

(A REVIEW OF SIXTY-SIX ADULT CASES WHICH OCCURRED IN THE 1937 ONTARIO EPIDEMIC)

By H. H. HYLAND, M.D., M.R.C.P., F.R.C.P. (C.), W. J. GARDINER, M.B., M.R.C.P.,
F. C. HEAL, M.D., W. A. OHLE, M.D. AND O. M. SOLANDT, M.D.

Toronto.

I.

DURING the late summer and autumn, 1937, Ontario suffered the worst epidemic of poliomyelitis in its history. Two thousand, five hundred and forty-four cases were reported,¹ with a mortality rate of 4.3 per cent and a paralysis rate of 56 per cent. During the previous ten years there were only 25 cases admitted to the Toronto General Hospital. Eighteen of these were admitted in 1930, the year of the last major epidemic in Ontario. Five deaths occurred in the 25 cases, representing a 20 per cent mortality. In the epidemic of 1937 sixty-six cases of poliomyelitis were admitted to the Toronto General Hospital, and the following report is based on a study of these cases. A number of other patients who were probably suffering from poliomyelitis were seen, but for the purpose of this survey only cases have been included in which the diagnosis was definitely established after taking into consideration the history, the presence of paralysis, and, in non-paralyzed cases, the findings on examination of the cerebrospinal fluid.

All the patients included in this series were 14 years of age or over, and the great majority were between 16 and 30 years of age. The number of male patients exceeded the females in a ratio of 1.86:1, which is a rather higher proportion than reported by other observers,² but approximates the recognized sex ratio.

Symptomatology.—The usual history was one of an abrupt onset with headache and stiffness

of the neck or back, and pain in the trunk or limbs. In less than 50 per cent of the cases the onset was insidious, commonly characterized by malaise, feverishness, mild congestion of the nose and throat, or by gastro-intestinal symptoms of

TABLE I.
AGE AND SEX INCIDENCE IN 66 CASES OF POLIOMYELITIS

Age groups	No. of cases	Sex	No. of cases
10 to 15	11	Male	43
16 to 20	30	Female	23
21 to 30	20		
31 to 40	4		
41 +	1		
Total	66		66
Oldest, 45 years			
Youngest, 14 years			

anorexia, nausea, vomiting, constipation or, infrequently, diarrhoea. It is interesting to note that three patients complained of pains in the chest as the initial symptom, and two of these subsequently developed respiratory paralysis. In one patient, a bulbar case, the initial symptom was one of difficulty in swallowing and talking which was related to paralysis of the palate and muscles of mastication and was not associated with any constitutional symptoms. The frequency of symptoms complained of during the course of the illness, other than those related to paralysis of skeletal muscles, is shown in Table II.

The 17 patients who had retention of urine were all severely paralyzed except in one instance where no paralysis ever developed. The urinary symptoms usually subsided in about ten days if the patient survived. However, one

* From the Department of Medicine, University of Toronto, and the Department of Physical Therapy and the Medical Service, Toronto General Hospital.

patient who had paralysis of the back and abdominal muscles had to be catheterized for three days, and difficulty in voiding persisted for three to four months. Three months after the onset examination showed ten ounces of residual urine and a hypotonic bladder.

Seven patients complained of abdominal pain, which was usually of a crampy nature. In one

TABLE II.

SYMPTOMS COMPLAINED OF DURING COURSE OF ILLNESS
IN 66 CASES

Symptoms	No. of cases
Headache	40
Back pain	34
Stiff neck and back	31
Vomiting	23
Malaise	19
Anorexia; retention of urine	17
Nausea	15
Constipation	12
Diarrhoea; feverishness; head-cold	8
Abdominal pain and discomfort; sore throat ...	7
Pain in legs	6
Dizziness; insomnia	5
Generalized aches and pains; pains in chest; gross mental upset	4
Pain in shoulders	3
Fatigue and tiredness; chills; restlessness and irritability; violent twitching in limbs; drowsiness; prostration	2
Blurring of vision; feeling of suffocation; stiff- ness of right arm; faintness; pain in right arm; tremor of hands; coma; frequency of micturition	1
No adequate description	2

of these a diagnosis of acute appendicitis was made and an operation performed. The appendix removed showed no evidence of acute inflammation on pathological examination.

Although it is the prevailing custom to attribute all the so-called constitutional symptoms to the virus affecting the central nervous system,³ symptoms definitely indicating cerebral involvement were not common. As will be seen in Table II, only a small number of patients showed gross mental upset. One of these had confusion, hallucinations and mania which persisted for several weeks. In addition to having muscle paralysis, this patient showed an upgoing toe on plantar stimulation, which later became normal. Other symptoms considered as encephalitic were vertigo, insomnia, drowsiness, and coma. Coma occurred in only one patient and developed twenty hours before definite evidence of paralysis was found. The temperature of the patient was 101° at this time. During the next two days it rose steadily and the patient died with hyperpyrexia—temperature 108°. At autopsy the brain showed oedema and con-

gestion, with numerous minute subependymal hæmorrhages in the right hypothalamus. The brain stem contained many small areas of hæmorrhage and focal necrosis.

Clinical manifestations during the early acute stages.—Fifty-seven cases were seen during the acute phase of the disease. Twenty-two of these patients were paralyzed on admission to hospital and 16 developed paralysis after admission; nineteen admitted during the acute illness never developed paralysis; the other 9 patients in the series, all of whom were paralyzed, came under observation during convalescence.

Table III shows the time of onset of paralysis in the 47 cases in which this condition developed. It will be noted that paralysis may appear as the first symptom or it may not become evident for several weeks after the onset of the disease. However, the majority of cases (70 per cent) developed paralysis within a week of the onset.

TABLE III.

DEVELOPMENT OF PARALYSIS IN 47 CASES IN
RELATION TO ONSET OF DISEASE

Paralysis developed	No. of cases	Percentage
With onset (bulbar)	1	70
1 to 3 days after onset	21	
4 to 6 days after onset	12	
7 to 10 days after onset	6	
11 to 20 days after onset	3	
21 to 30 days after onset	2	
Time not definitely known	2	

In only 3 cases was there a clear-cut history of a remission during the acute illness. The remission varied from one to three days, illustrating the so-called "dromedary" type of the disease.

Practically all the patients looked acutely ill on admission to hospital. Many showed flushed faces and bright eyes, with a terrified, anxious expression. In almost all cases stiffness of the neck and back was demonstrated and the patients resented being examined. Positive Kernig or Brudzinski signs, or both, were usually present. Seventeen cases showed well-marked muscle tenderness, frequently confined to localized areas. Although this sign was often a precursor of paralysis, yet several of the patients never developed paralysis of the affected muscles. When hyperæsthesia and muscle tenderness are extreme it may be difficult to be sure whether finer degrees of weakness exist. Twitchings and tremor were seen in the limbs of only 3 patients and all three subsequently became paralyzed.

These symptoms appear to be much less common in adults than in children.

Of the 19 cases with bulbar involvement 10 showed difficulty in swallowing, 6 showed impairment of phonation, 1 had diplopia, 5 had nystagmus, and 1 had difficulty in chewing. On examination, definite evidence of paralysis of the muscles supplied by one or more of the 3rd, 5th, 6th, 7th, 10th, 11th and 12th cranial nerves was seen in these cases. Involvement was commonest in muscles supplied by the 10th, 7th and 5th nerves respectively.

In view of the interest stimulated by the evidence that in monkeys the poliomyelitis virus enters the central nervous system *via* the olfactory nerves,^{4, 5} and that a zinc sulphate nasal spray is of prophylactic value in these animals,⁶ it was thought worth while to test the sense of smell quantitatively in a number of acute cases. An olfactometer was prepared, similar to that devised by Elsberg,⁷ and the technique recommended by him was followed. In conjunction with Dr. P. E. Ireland, of the Oto-Laryngological Service, 30 cases in the acute stage of poliomyelitis and 19 controls of approximately the same age group were examined, using ground coffee as the test substance and the blast method of injection.⁷ Where the nasal passages were found to be obstructed the tissues were shrunk with ephedrine spray before testing. The results showed that in 22 cases of poliomyelitis appreciation of odour was normal bilaterally. In 4 cases where a definite nasal lesion, such as deviated septum or enlarged turbinates, was present the appreciation was impaired, but these cases were considered as questionable. In 4 cases appreciation of odour was definitely below the normal. In the control group, 15 cases had normal appreciation of smell bilaterally. There was one doubtful case and three with definitely defective appreciation for which no cause could be found. From these results it was concluded that no significant defect in the olfactory sense is associated with the acute phase of poliomyelitis.

While a more detailed discussion of the distribution of paralysis will follow later, it is well to emphasize here that in the acute stage of the disease when paralysis is developing the chief concern should be early detection of involvement of the respiratory muscles. When paralysis occurs bilaterally in the shoulder girdles, neck, back and/or abdomen, the onset of respira-

tory difficulty may be rapid owing to the associated involvement of intercostals and diaphragm. Weakness of the muscles may progress to an appreciable degree before patients voluntarily complain of difficulty in breathing or show gross evidence of respiratory insufficiency, such as cyanosis or the operation of the accessory muscles of respiration. It is important to observe patients of this type very carefully, not only to prevent a fatality occurring from rapid development of severe paralysis of the respiratory muscles but also in order that respirator treatment may be instituted early in the hope that the consequent rest to the muscles may limit the progression of the respiratory paralysis.

Early diaphragmatic weakness can best be detected by observing whether on forced inspiration the outward movement of the upper abdomen can be limited by gentle pressure of the hands. More advanced weakness can be recognized by inspection of the abdomen on inspiration. A similar method for the detection of early intercostal weakness gives information which may not be obvious by inspection. The patient may appear to be breathing quite well but, when manual resistance is offered to the movement of the chest, intercostal weakness can sometimes be noted.

In 60 cases, where temperature records during the early days of the illness were available, fever was found in 58. The 2 cases with no fever (both paralytics) were not admitted to hospital until six days after the onset of their illness. The usual finding was a variable fever during the first four days, showing an average maximum of about 102°. Hyperpyrexia (above 105°) only occurred as a terminal event in fatal cases. Temperatures above 103° were rare except in cases with respiratory paralysis, where the temperature sometimes was elevated to above 104° with subsequent recovery.

Paralysis usually developed when the patient was febrile and did not progress after the fever subsided. It was not unusual, however, for the maximum paralysis to occur when very little fever was present, and occasionally after the temperature had returned to normal. Persistent low-grade fever was noted in a few cases and in three instances continued for months without an obvious cause being found. It is possible that this persistent fever was due to the effects of the disease causing an imbalance of the central heat-regulating mechanism.

Cerebrospinal fluid examinations.—The cerebrospinal fluid was examined after admission to hospital in 47 cases, which included all but one of the non-paralyzed cases. Spinal puncture had been performed before admission in this case, and positive findings were reported. Lumbar puncture was not done on 18 of the paralyzed cases where the clinical findings were sufficiently definite that spinal fluid examination was not deemed necessary to corroborate the diagnosis.

Table IV shows the cell counts in 29 cases where paralysis was present on admission or developed later, and in 18 cases where paralysis never developed. In general, the cases with paralysis showed a greater incidence of higher counts, 73 per cent showing between 50 and 500 cells; of the non-paralyzed cases 50 per cent had counts of 50 cells or less. Only one non-

TABLE IV.
CEREBROSPINAL FLUID CELL COUNTS IN 47 CASES

29 paralyzed cases		18 non-paralyzed cases	
No. of cells	No. of cases	No. of cells	No. of cases
0 to 4	1	0 to 4	0
5 to 50	5	5 to 50	9
51 to 100	7	51 to 100	3
101 to 250	6	101 to 250	1
251 to 500	8	251 to 500	1
501 to 1000	2	501 to 1000	2
		1001 to 2000	1
		2001 +	1

paralyzed case had a cell count below 15. This patient showed 5 cells on the third day after the onset, and the diagnosis of poliomyelitis was based on a very typical history and the findings on examination of the limbs of a definite difference in reflexes on the two sides which disappeared within four days. The highest counts, 1,250 and 2,500 cells, were found in two patients who never developed paralysis. The signs of meningeal irritation were slight in both cases. The latter count was made on spinal fluid taken five days after the onset of the disease and subsequent examination, two days later, showed 911 cells. Spinal puncture in the former case was done the day of onset, and twenty-four hours later was repeated, with a finding of 250 cells. In two paralyzed cases cell counts within normal limits were obtained. In one case with a typical history and a left facial paresis lumbar puncture four days after the onset showed two cells. In the other case two spinal fluid examinations, one and two days after the onset respectively, were within normal limits. Paralysis developed four

days after the onset and lumbar puncture done on this day showed 350 cells to be present. One non-paralyzed case showed a cell count of four the day after the onset, but two days later a second lumbar puncture showed 32 cells.

The above observations suggest that the cell count in the cerebrospinal fluid can alter materially in a relatively short period of time, and that the number of cells is not an accurate index of the degree of involvement of the nervous system. Negative cerebrospinal fluid findings in the early stages may be misleading, and too much reliance should not be placed on them in the presence of other evidence of the disease.

In all cases with elevated cerebrospinal fluid cell counts lymphocytes predominated and the proportion of polymorphonuclears was usually small. An increase of globulin was in no case very marked, and in many the Pandy test revealed slight or no increase. No significant changes in cerebrospinal fluid pressure were observed.

White blood cell counts were done on twenty-seven cases in hospital. In eighteen cases leucocytosis of over 10,000 was present; in only two cases, however, was the count over 15,000, the highest being 18,300 in a fatal case. Six of the nine cases with a leucocyte count under 10,000 were paralyzed.

CLASSIFICATION

The paralyzed cases have been divided into three groups—bulbar, spinal and bulbospinal. The incidence of these three types is shown in Table V.

TABLE V.
INCIDENCE OF PARALYSIS IN 66 CASES OF POLIOMYELITIS

	No. of cases
No paralysis	19
Paralysis	47
Paralysis of respiratory muscles.....	18 (38 per cent)
Type of paralysis:	
Bulbar	3
Bulbospinal	16
Spinal	28

As will be seen from the table, 19 patients had involvement of the brain stem. In 3 of these the evidence of paralysis was limited to this region. One of the three had severe paralysis of the muscles of phonation and deglutition; vomiting of blood occurred, and death ensued from the aspiration of blood. One other patient, who made a complete recovery, had moderate

involvement of the muscles of deglutition and phonation. The other patient had only mild paralysis of the facial muscles and also made a complete recovery.

Nine of the 16 patients with paralysis indicating involvement of the brain stem and spinal cord (bulbospinal) had extreme difficulty in swallowing as the most serious manifestation of their bulbar paralysis. Seven of these patients died during respirator treatment. The other 2, both respirator-treated cases, recovered completely from the bulbar symptoms. Of the remaining 7 bulbospinal cases 4 had difficulty in swallowing of moderate degree and brief duration. Two of the other three cases had paralysis of masticatory muscles; the other showed facial paralysis as the predominant manifestation of bulbar involvement.

Distribution of paralysis.—The distribution of paralysis in the 47 paralyzed cases is shown in Table VI.

TABLE VI.
DISTRIBUTION OF PARALYSIS IN 47 CASES,
TORONTO GENERAL HOSPITAL, 1937

<i>Muscles affected</i>	<i>Degree of paralysis</i>			<i>No. of Cases</i>
	<i>Severe</i>	<i>Moderate</i>	<i>Slight</i>	
Muscles supplied by cranial nerves (nystagmus was present in 5 cases).....	5	6	8	19
Neck muscles	6	4		10
Left upper limb.....	17	11	8	36
Right upper limb.....	14	9	6	29
Chest muscles (intercostals and diaphragm)	15	2	1	18
Abdominal muscles	15	5	1	21
Left lower limb	16	7	10	33
Right lower limb	15	9	4	28
Back muscles	13	11	2	26
Paralysis confined to:				
One limb				7
Cranial nerves				3
Abdominal muscles				1
Trunk muscles				1

It will be noted that the muscles of the left upper limb were involved most frequently. A predominance of paralysis in the left arm has been noted by others.⁵ In the upper limbs the proximal muscles showed the greatest frequency and severity of paralysis, the deltoid being the most constantly involved. The incidence of paralysis in the hands was not so great, but the opponens pollicis muscle was particularly prone to be affected and in a number of cases was severely paralyzed. In the lower limbs the proximal and distal groups of muscles seemed to be affected about equally, but the paralysis

causing the major disability occurred in the dorsiflexors of the feet. In the trunk the muscles of the back, abdomen and chest were involved in that order of frequency, and, in cases where respiratory muscle paralysis occurred, there was invariably associated weakness of the back and abdominal muscles and usually also widespread paralysis in the upper and lower limbs.

MORTALITY AND POST-MORTEM FINDINGS

Nine deaths occurred in this series of 66 cases. One case was a pure bulbar, 7 were bulbospinal, and 1 was a spinal type. They all died within two weeks of onset of their illness, and in 6 instances death occurred within three days of admission to hospital. Eight had respiratory paralysis and 7 of these were treated in respirators. The bulbar case suffered from epistaxis and hæmatemesis the day of death, and it was felt that aspiration of blood into the larynx and trachea determined the fatal outcome.

Six cases came to autopsy, all of which had severe, widespread paralysis including the respiratory muscles and had received respirator treatment. All showed pulmonary collapse of varying degrees. One case which developed laryngeal paralysis before death showed massive collapse of both lower lobes, which was attributed to mucous plugs which were found in the bronchi. Definite bronchopneumonia was found in 5 cases. In the other case passive congestion of the lungs, with purpuric hæmorrhages in the pericardium, gastric mucosa and periaortic tissues, was present. No gross or microscopic evidence of emphysema was found at post-mortem examination in the 6 respirator-treated cases. This differs from the findings of Brahdý and Lenarsky,⁹ and Wilson,¹⁰ who reported gross and microscopic emphysema in several of their respirator-treated fatal cases.

All the fatal cases showed marked œdema and softening of the spinal cord, most pronounced in the gray matter. In 5 cases petechial hæmorrhages were present in the cord. Microscopic examination of the spinal cord showed the characteristic findings associated with severe poliomyelitis. There was œdema of the brain in all 6 cases, and in 5 necrosis and petechial hæmorrhages were present in the brain stem. Inflammatory changes were found in the hypothalamic region in all cases, but no definite cortical lesions were detected.

TREATMENT

In discussing the treatment which was adopted in this series of cases consideration will be given to three aspects—immediate measures, serotherapy, and the after-care of the paralytics. Descriptions will be included of the special methods used in the handling of various types of cases.

Management of patients during the acute stage of the disease.—When it became evident that an epidemic of serious proportions was developing a wing of the hospital was isolated for the purpose of housing poliomyelitis cases. The attendants observed the ordinary precautions, and it is noteworthy that none of them contracted the disease.¹¹ When the diagnosis of poliomyelitis was established in a given case the patient was put at complete rest in bed and carefully examined for any evidence of muscle weakness or paralysis. If such was found the paralyzed muscles were supported with sandbags and pillows. Slings and cradles were used to relieve the strain which would otherwise be imposed by gravity or the weight of the bed clothes. No massage was attempted until the temperature was normal or until the hyperaesthesia and muscle tenderness had subsided or become mild. Passive movements of the limbs were instituted early to counteract the stiffness of the joints, which may develop so rapidly, and to improve the circulation in the limbs. During this stage, where the muscle paralysis was of sufficient degree to warrant splints, the specifications for their manufacture were obtained. The criterion for the use of splints was the inability of the weakened muscle or group of muscles to carry out their full range of movement against gravity. If the muscle or muscles could perform their full range of movement, even though weakly, it was usually considered adequate to give support by means other than splinting, such as slings, pillows or sandbags.

Particular attention was paid to the care of the skin over pressure points, to prevent bed sores, such as are prone to occur in the areas where paralysis is present and where nutrition of the skin is poor.

Serotherapy.—Twenty-six of the 66 cases were treated with convalescent serum in the pre-paralytic stage. The following table shows the results in serum-treated cases compared with 32 controls of approximately the same age group.

TABLE VII.
SERUM-TREATED CASES AND CONTROLS

	No. of cases	Percentage
Serum administered in pre-paralytic stage		
Paralysis developed	17	65
No paralysis	9	35
Died	3	
Controls: serum not given	32	
Paralysis developed	22	69
No paralysis	10	31
Died	3	

It will be noted that the percentage of cases developing paralysis after the administration of serum is practically the same as that which occurred in the control group where no serum was given.

Of the 26 pre-paralytic cases in which serum was administered 14 received 100 c.c. intravenously; 4 were given 50 c.c. intramuscularly; 2 were given transfusions from convalescent cases; and the remainder received 25 c.c. intramuscularly. The amount or method of administration of the serum did not appear to influence the course of the disease in these cases. Of those receiving 100 c.c. intravenously 3 developed widespread paralysis and died of respiratory failure. Those patients who developed paralysis after serum treatment did so in varying periods of from twelve hours to fourteen days, the majority in from one to five days. In 17 cases serum in amounts from 50 to 200 c.c. was given after paralysis developed, but this method did not appear to have any effect on the fever or on the progression of paralysis.

While the series of serum-treated cases and controls is small, it is our impression that the administration of serum in poliomyelitis has no effect in preventing paralysis or in modifying the course of the disease. This opinion is essentially the same as that held by Park,¹² and Kramer, Aycock and associates,¹³ both of whom reported a large series of serum-treated cases and controls.

Management of cases with respiratory paralysis.—A number of our cases developed some degree of respiratory paralysis, and we were confronted with the problem of carrying out artificial respiration until the patient either died or was able to ventilate himself adequately. Numerous types of machines have been developed for use in the treatment of patients suffering from respiratory distress. Several were used during the epidemic, but in our ex-

perience the Drinker^{*14} type of respirator was by far the most effective for treatment during the acute phase of the illness and in cases where prolonged treatment was necessary.

Cases manifesting respiratory difficulty may be divided into three groups: (1) spinal, with paralysis of intercostals or diaphragm, or both; (2) bulbar, where the respiratory and cardiovascular centres may be affected; (3) a combination of spinal and bulbar types.

The management of spinal and combination types was essentially the same. There is still some question as to the optimal time to place these patients in respirators. Brahdry and Lenarsky^{9, 15} are inclined to institute artificial respiration only in advanced cases, basing their view on the fact that, of 27 patients surviving respirator treatment 12 died of pulmonary disease, either massive collapse or bronchopneumonia, at intervals of two weeks to two years after their removal from the respirators. Wilson,¹⁰ however, institutes respirator therapy when early signs of respiratory paralysis are evident, but if this was done during an epidemic many respirators would be necessary. We are of the opinion that a person with a vital capacity reduced to approximately 1,500 c.c. is benefited by treatment in a respirator. Certainly, if any of the signs or symptoms of respiratory distress are present, such as cyanosis, dyspnoea with use of the accessory muscles, difficulty in talking, fatigue induced by rapid laboured breathing, marked limitation of movement of the chest or diaphragm, immediate institution of respirator treatment is indicated. Bulbar cases have a bad prognosis whatever mode of therapy is used, but there is no contraindication to placing these patients in respirators if signs of respiratory distress are evident. It is important to have the foot of the respirator raised about 20°, to turn the patient frequently, and to employ the methods described elsewhere in treatment of bulbar paralysis.

With the Drinker type of respirator adults were most comfortable when eighteen to twenty respirations were induced per minute; in younger patients somewhat faster rates were better (twenty to twenty-eight per minute).

* The "Drinker" respirators used in the treatment of these cases were supplied by the Provincial Department of Health of Ontario. The majority of these were built in the Hospital for Sick Children, Toronto, and the remainder in the Toronto General Hospital. To all concerned in making these machines available so promptly we wish to express our grateful thanks.

The degree of negative pressure to be used depends on the individual case. With the most severe degrees of paralysis in adults a negative pressure of 25 cm. of water was found to be adequate; when the chronic stage was reached a pressure of 15 cm. was usually sufficient. In children the negative pressure should not exceed 10 to 15 cm. and, in adults, 30 cm. is the upper border of safety. It has been shown that excessively large negative pressures (over 30 cm. in an adult and 15 cm. in a child), if used over a period of time, tend to produce emphysema.¹⁶ One should aim at maintaining as low a pressure as is compatible with comfortable respirations for the patient.

There appears to be no danger of producing alkalosis or tetany if the above general principles are followed. Should the patient not breathe in unison with the rhythm of the respirator, or if he is apprehensive, an adequate dose of morphine should be given. Sedatives are not required for long as most adults soon learn to cooperate with the machine.

There are several main causes of death in respirator-treated cases, and it was with the hope of preventing these that special medical and nursing care was employed. First, the patient may die of his disease either through a depression of the cardiovascular and respiratory centres or from the generalized toxæmia. The prognosis is grave in these cases and stimulants have little or no effect. Second, pneumonia may result from an acquired upper respiratory infection. To aid in preventing this, attendants always wore masks. No one with an upper respiratory infection was allowed to visit the patients, and the patients were protected from exposure to draughts, etc. An endeavour was made to keep the airway clear and to lessen excessive secretions so as to minimize the danger of aspiration of extraneous material during machine-induced inspirations. The patients were taught to eat and drink with the machine in operation. When this could not be accomplished the machine was stopped while food was being taken. The foot of the respirator was elevated 20° to aid postural drainage. Suction was carefully employed, to avoid damage to the nasal and pharyngeal mucous membranes. Trays set up with a laryngoscope, intratracheal catheters, and a bronchoscopic outfit were always available in the event of a patient aspirating material and thus developing massive collapse

or sudden laryngeal obstruction. The patients were turned from side to side and put face downward at frequent intervals in the hope of reducing the degree of pulmonary collapse.

Bed sores are very prone to develop rapidly and may lead to a fatal outcome. From the beginning pressure points were protected and the skin over these areas given proper attention. As most patients suffer from retention of urine, frequent catheterization may easily result in genito-urinary infections unless the most rigid precautions are observed. Intractable constipation followed by severe nausea, vomiting, and distension can usually be prevented by the judicious use of mineral oil, laxatives and enemata. In persistent vomiting a duodenal tube employed for gastric lavage and to instil fluids and nutriment is of value.

To care for a patient in a respirator properly it is important to have a trained team of doctors, nurses, physiotherapists and other attendants to thoroughly and efficiently bathe the patient, care for the skin, change bed linen, catheterize, administer enemata, apply physiotherapy and any necessary medical treatment, all in the short interval that the patient is able to be out of the respirator. For our group of respirator cases a detailed schedule was drawn up concerning the times and the intervals that patients were to be out of the machines. The care and treatment employed each time out were recorded not only to ensure adequate attention to the individual but in order that the entire group might receive efficient attention. Extreme muscle tenderness and hyperæsthesia, which is often severe and may be protracted in these cases, necessitates particular gentleness in handling.

Many patients, especially during the acute stage, and possibly for some months, are able to remain outside their respirators only for a few minutes without the administration of oxygen. Prolonged use of the nasal catheter is dangerous, as it may induce inflammatory changes in the upper respiratory tract which may extend downward resulting in fatal bronchopneumonia. We were able in the most severe cases to keep patients out of the respirators comfortably for half-hour intervals by employing artificial respiration with a Forreger anæsthetic machine, using high concentrations of oxygen. This was found necessary in cases with vital capacities under 300 c.c. In patients with vital capacities

of 300 to 500 c.c. an ordinary mask of the type used on McKesson anæsthetic units connected to an oxygen tank was very efficient. Patients with vital capacities over 500 c.c. could usually remain outside their machines comfortably for at least half an hour.

Patients were removed from the respirators at least three times in twenty-four hours for routine nursing care, medical attention, and, later, for physiotherapy treatments. Much can be done to increase the general comfort of the patient by using air-mattresses, large and small rubber rings with pads under pressure points, frequent changes of position, and very light massage. The rubber collars, if not adequately padded, may produce sores around the neck.

The general treatment of poliomyelitis is the same whether the patient is in bed or in a respirator, but adequate treatment of the paralyzed limbs may be difficult to administer to respirator cases. The width of the respirators did not permit the use of abduction splints on the arms, so on every occasion when the patient was out of the machine his arms were placed in abduction, to give some relaxation to the deltoids and also to prevent contractures in the pectoral girdles. Unless particular care is taken the patient will be placed in the machine with his arms folded across his chest. This is liable to stretch a weak triceps, and might, therefore, predispose to the development of contractures in the biceps. The arms should be in a position of almost complete extension at the elbows during most of the time that the patient is in the respirator, and carefully supervised physiotherapy should be applied to the arms and shoulder-girdles on every possible occasion.

Management of bulbar cases.—In cases with bulbar involvement difficulty in swallowing and the collection of excess mucus in the throat were the major problems in treatment. Special nursing care and the discontinuance of food and fluids by mouth were instituted at once. Methods designed to cope with excess mucus included elevating the foot of the bed, hypodermic injections of atropine in repeated doses, and the use of suction apparatus. Sedatives, such as sodium luminal intramuscularly, were administered to allay the patient's apprehension. Fluids were given intravenously or by duodenal tube when deemed necessary. In certain of the bulbar cases and in some cases where headache was a very prominent symptom the administra-

tion of 50 per cent glucose, in 50 c.c. doses intravenously, was used in the hope of reducing œdema associated with the infection in the central nervous system. There appeared to be some relief of the headache and, occasionally, some temporary improvement in bulbar symptoms, but it was not definitely established that this treatment was of any value in retarding progression of the disease, once paralysis had occurred.

The management of non-paralytic cases.—Non-paralytic cases were usually discharged from hospital at the termination of the three weeks' quarantine period. However appointments were made for these patients to be re-examined within four weeks of discharge, and they were instructed to communicate with us should any untoward symptoms develop. In several instances these non-paralytic patients, in common with a few with slight paralysis, were inconvenienced by persistent pains in various muscles of the limbs or back. These pains were usually aggravated by exertion. In three cases they were sufficiently severe to require a period of complete rest and ultra-short-wave diathermy was administered over the region of the cord where it was assumed that the inflammatory change leading to the pains was present. With this treatment the pains ultimately disappeared in every case. In patients who were discharged from hospital as non-paralytic subsequent examination did not reveal any instances of paralysis which had developed following return to normal activity.

The treatment of paralytic cases during convalescence.—After the quarantine period was over the majority of the paralyzed patients remained in hospital, and all were kept at complete rest in bed. Where there was well marked paralysis of the back or girdle muscles Bradford frames or fracture boards were used in the early stages.

Prevention of deformities depends on accurate and repeated observations of the extent of the paralysis and on the early detection of more rapid recovery in certain muscles in order that consequent over-stretching of their weak antagonists may be prevented. This is liable to occur and if allowed to continue unchecked may rapidly lead to the development of severe contractures and, possibly, to irreparable damage to the stretched muscles.

For the best results in the treatment of paralytic cases the findings obtained on repeated examinations should be carefully recorded in a manner which permits comparison at different periods during convalescence. This makes it possible to gauge accurately the progress and to make necessary modifications in treatment. For this purpose a printed chart* on which all the important muscles are listed is invaluable. Examinations should be charted once monthly. These detailed records of the state of the affected muscles serve as a guide for the general management of the case and indicate the particular muscles requiring more frequent observations.

For the purpose of more accurately recording improvement in paralyzed muscles repeated estimations of the returning power were made with spring balances. Two of these instruments were used, one graduated in ounces and the other in pounds. It was found that almost all the limb muscles could be examined by attaching slings to the limbs in an appropriate manner and having the patient voluntarily maintain the limb in position by means of the muscles or group of muscles to be tested against the spring balance.

Suitable splints of an easily adjustable type were applied where necessary. Those most commonly used were designed to keep the feet in dorsiflexion and the arms in abduction at the shoulders. Bivalved plaster casts were used very little because they were found to be less clean and comfortable, and they tended to cause pressure sores. Thin, flat, plaster splints were found effective in dealing with paralysis of the extensor muscles of the wrists and fingers.

Various types of splints were tried in the treatment of opponens pollicis paralysis. The most effective was a glove cut so that the fingers were free but the thumb kept in correct position by means of a roll support in the palm of the hand and tied to a ring attached to the ulnar side of the glove. Less commonly used splints were devised according to the needs of the individual case. An example of such a splint is a tight abdominal binder in cases where severe paralysis of the abdominal muscles is present. Not only does this give support to the weakened muscles but it greatly facilitates coughing, defæcation and micturition.

* A copy of the chart used at the Toronto General Hospital may be obtained on application to the authors.

Occupational therapy.—From the first it was realized that the mental attitude of the patients must receive the greatest consideration. Much could be done by the doctors and nurses to create an atmosphere of optimism, but it was evident that means must be provided for occupying the patients' time in an interesting manner. In this regard the work of the occupational therapists has been invaluable. Various forms of activity suitable to the individual patients, according to age and temperament, were devised, and this method has been found most satisfactory in helping to maintain a healthy mental attitude in the paralyzed patients. The respirator cases presented the most difficult problem, but the installation of radios, the use of mirrors to enlarge their view of the ward, and the attachment of book-rests to the respirators, to make reading possible, have been of great value. A period of time each day has been devoted to the continuance of school work with those patients of school age who have remained in hospital. Educational authorities have cooperated by sending teachers to the wards to direct and supervise the studies. Up to the present time the emotional status in this series of patients has been consistently good, and it is probable that the care which has been taken to occupy their time in a pleasant and profitable manner has been instrumental in bringing this about.

Physiotherapy.—This series of cases received, in addition to rest and splinting, treatment by heat, massage, passive movements, active exercises, muscle training and galvanic stimulation. The purpose of such a program was as follows: (1) the prevention or retardation of the development of muscle atrophy; (2) the prevention of the development of contractures and deformities; (3) the re-education of the patient in the use of muscles recovering from paralysis; (4) in cases of muscle paralysis beyond recovery to educate the patient how to use his remaining muscles to the best possible advantage.

It is obvious that the best chance of accomplishing these objectives is by starting treatment early. Consequently, as soon as the patient's temperature was normal and the tenderness had disappeared from the affected muscles physiotherapy was commenced. Early treatment consisted of the application of heat, massage and passive movements. A portable lamp producing a non-luminous type of infra-red ray was the

source of heat. This was used for the purpose of increasing arterial circulation and relaxing muscle spasm. In the acute stage the latter was encountered not infrequently in unparalyzed antagonistic muscles. Arm and leg baths, with the water at 95° F., were also utilized for the same purpose.

Massage, at first, consisted of movements light in type. Effleurage, gentle kneading, and light friction were employed about the joints. The object of massage is primarily to aid the nutrition of the paralyzed muscle by increasing arterial circulation and venous and lymphatic drainage. Treatment at this stage should be brief, as over-treatment can produce paralytic dilatation of the capillaries, thus defeating the purpose of the massage. Affected extremities often can be treated while resting on splints but, if these are removed, adequate care must be taken that there is no stretching of paralyzed muscles. Although treatment is of short duration, it may be repeated two or three times during the day.

Passive or relaxed movements were used from the first. These have as their object the prevention of contractures and the preservation of mobility in the joints. Each joint was moved once daily, always exercising great care not to stretch paralyzed muscles. If two antagonistic groups of muscles were paralyzed, then passive movement was only carried out in the middle range.

Active movement is probably the most important single factor in the program of physical treatment, calling into play and exercising the entire neuro-muscular unit. Muscle training was commenced as soon as the slightest sign of voluntary contraction could be seen in the muscle. A definite plan was followed, commencing with gently assisted active movement, then advancing to free movement, and finally employing eccentric or concentric resisted active movement. In order to place the muscles in the best possible position for working, the sling method described by Guthrie-Smith¹⁶ was utilized. This consists of an overhead frame with canvas slings suspended from it. These are so arranged that an arm or a leg, or the whole body if necessary can be suspended in slings. This method possesses the advantage of eliminating friction and greatly decreasing the effect of gravity, and any type of active movement can be carried out. It is next in value to hydrotherapy (pool or Hub-

bard tank) and is of greatest assistance in treatment when the latter is not available.

Respiratory or breathing exercises were also used in patients recovering from paralysis of the muscles of respiration and able to be out of the respirator for varying periods of time. These exercises are specially designed to give active exercise to all the muscles of respiration.

Galvanic stimulation possesses value as a means of producing artificial exercise of a muscle. It should be used with great care, due to the ease with which muscle fatigue can be produced. The surging galvanic current was used with discrimination in these cases, chiefly where atrophy was developing rapidly or where mild contractures were appearing.

In the treatment of paralyzed cases by means of physiotherapy certain fundamental principles of muscle re-education must be kept in mind. (1) The masseuse must make sure that the patient understands what is required in the way of active movement. It may be necessary to demonstrate this either by means of a passive movement or by movement of a sound limb. (2) Fatigue of the muscle must be avoided. This will necessitate periods of rest between exercises or alternative massage and active movements. Evidence of fatigue will be seen as loss of power and contractility. When this occurs the muscle or muscle group should be rested for a few days, then active exercise resumed in a graduated manner. Anyone who has treated a large number of cases with active movement will have made this observation; if not, then the amount of active exercise has not been carried to the desired degree which is just slightly less than the maximum. (3) A paralyzed muscle must never be stretched by the contraction of a muscle undergoing active movement. (4) One should remember not to neglect the muscles of a non-paralyzed extremity, which frequently suffer from prolonged rest in bed.

The necessity for close clinical observation of the recovering paralytic cases cannot be over-emphasized. Methods of physiotherapy have to be altered or modified repeatedly if the maximum recovery is to be obtained. It has been observed frequently that in a given case the muscles may improve rapidly for a time and then improvement will cease, only to be resumed when the necessary change in treatment is made. The following case serves as an illustration.

B.M., male, aged 17, was admitted to hospital on September 5, 1937.

The patient had almost complete paralysis of the whole left arm and severe paresis of the whole right arm and right leg. His left leg showed only mild paresis. He was placed on a Bradford frame and the left arm maintained in an abduction and flexion splint with support to the wrist. The right arm was maintained in an abduction splint with extension at the elbow. The feet were supported in dorsiflexion. Physiotherapy was commenced on September 28th and consisted of infra-red radiation to the paralyzed limbs followed by massage, passive movements at all joints, and muscle training.

On October 28th contractures were found to be developing in the right arm at the elbow. The splint was removed from the arm and controlled active exercises were instituted. Following this there was rapid improvement in power and recovery from the contractures. The right *opponens pollicis* muscle was splinted on October 28th. On October 31st sling exercises for both arms were instituted and hot water baths to the left arm. In addition to infra-red radiation and massage active exercises were commenced for the back and legs.

By November 18th improvement in the right arm had progressed rapidly, but the left arm showed very little improvement. The legs were improving slowly. There was no improvement in the right *opponens*; it was paralyzed to about the same degree as the left. The right *opponens* splint was removed and the muscle treated with active movement while the left *opponens pollicis* was splinted.

On November 23rd splinting of the left arm was abandoned because of fixation of inward rotation at the left shoulder, and treatment by controlled active movements was increased. On November 29th the contractures at the left shoulder were much improved. By December 16th the right arm and the left leg were improving very satisfactorily, and the left arm showed return of power in certain muscle groups. The left wrist extensors, however, which had previously displayed fair power, were found to be powerless. This was attributed to too much active movement, so a cock-up splint was applied and active movements stopped. By December 28th the power had returned to the extensors of the left wrist and the movement was strong once more, but since wearing the cock-up splint stiffness of the wrist on flexion had developed.

Examination on January 17th showed the right arm to be almost normal in power, except for the *opponens*, which, although still weak, was improving. The left arm showed much improvement particularly in the proximal muscles; the *opponens*, however, had no power. The legs were almost normal, apart from a mild weakness of the toes. The extensors of the left wrist were still improving in power but, although the stiffness of the wrist joint was now almost negligible, the power of the flexors, which formerly had been quite good, was poor. They apparently had suffered as a consequence of the extensor splinting.

The left arm had been supported in abduction for about five weeks by pillows and a sling, and, on January 24th, a contracture of the left trapezius and a mild scoliosis of the upper thoracic spine were noted. Abduction of the arm was discontinued and sandbags were applied to the left shoulder.

On February 14th, exercises for mobility and strengthening of the back were instituted, together with general exercises for the whole body. The only serious paralysis remaining at this time was in the left arm, but some voluntary power was present in every muscle except the *opponens*.

By February 22nd the contracture in the left trapezius was much improved and the scoliosis scarcely apparent. Power in the left deltoid and left shoulder-girdle muscles had not shown any regression since the support was removed. However, a tendency to contracture in the left pectoral muscles was noted, and it was planned to abduct the arm for twelve hours each day.

Examination on March 22nd showed no contracture and improvement had progressed in all muscles of the left arm except the opponens pollicis.

The progress of this case clearly shows the need of careful examination of the paralyzed patients at short intervals and of the necessity for modifying or altering the treatment in order to prevent deformities and to facilitate the recovery of the paralyzed muscles. It shows, too, that no general plan of treatment, no matter how complete, can be adopted for all cases.

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(To be continued)

EXPERIMENTAL STUDIES WITH SULPHANILAMIDE AND OTHER COMPOUNDS*

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THE introduction of chemical compounds for the treatment of bacterial infections has always been characterized by the great enthusiasm of the sponsors. Because only a very few have stood the test of time a justly sceptical attitude has been developed towards the acceptance of specific chemo-therapeutic agents. Sulphanilamide and other compounds have been widely acclaimed as remarkably efficient therapeutic drugs. Full evaluation of their clinical effectiveness, limitations and dangers is far from complete, but it is certain that in their present form they should not be used for all bacterial infections.

The basis for the clinical use of these drugs was the experiments of Domagk¹ conducted in 1932. His results were not published until February, 1935, so that the earliest papers to appear on this subject were clinical. The first drug, patented on Christmas Day, 1932, by

Domagk, was named streptozon, to indicate, we presume, that it was specifically active against streptococci. Strangely enough, though, the first case treated with streptozon was one of generalized staphylococcal infection of the skin. Improvement followed the treatment. Neither this paper nor those that followed in the next two years aroused any interest, and it was Domagk's publication that first stirred scientific thought.

Domagk's investigations were prompted by the observation that for an aniline dye to be fast for fabrics it must have a double nitrogen linkage between a benzene ring and a sulphonamide radical in the para position. Someone suggested that such compounds might have a destructive action on bacterial protoplasm. Domagk therefore infected animals with a number of pathogenic bacteria and treated them with all the aniline dyes having this structure. He found that mice survived a hæmolytic streptococcal infection if they were treated with the substances now known as the prontosils. Prontosils have no effect upon hæmolytic streptococci in the test tube. Thus there was no ready ex-

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planation of the curative effect, and had the *in vivo* test not been used these drugs would not have been discovered.

Experiments by a group of French workers demonstrated that the double nitrogen linkage was not essential and that the simpler compound, para-amino-benzene-sulphonamide, named by Fuller sulphanilamide, was just as effective. This substance which had been known for thirty years, was shown to inhibit the growth of streptococci *in vitro*, and could be liberated from the prontosils by reduction. The curative effect of the prontosils was supposed to be due to bacteriostasis through conversion in the body to sulphanilamide. Considerable confusion has occurred in the literature through the use of the name "prontosil" for all three compounds. In many publications it is almost impossible to determine which one of the drugs was used for treatment. Adequate comparison of the clinical efficiency of these drugs, in many instances, cannot be made because of this terminology.

EXPERIMENTAL

Certain conditions are necessary before therapeutic effects can be demonstrated with these drugs in experimental animals. The particular bacterial species used for infection is very important, and the strain must be virulent for the type of animal injected in order that dramatic results may be obtained.

Streptococci.—Many strains of hæmolytic streptococci freshly isolated from human infections have a low virulence for white mice. Doses of 10 million bacteria, injected intraperitoneally, usually are necessary to cause the death of the animals. If such strains are transferred repeatedly through mice the virulence of some will become enhanced so that the injection of 20 or 30 streptococci will kill 90 per cent of the mice.

Working with a strain of this virulence, very remarkable results can be obtained on treating either with the prontosils or with sulphanilamide. White mice can be infected with as many as 10,000 lethal doses of hæmolytic streptococci and at least 80 per cent of them be saved by the drugs. All of the control mice will die in 24 or at the latest 48 hours. Mice can be protected even though treatment be delayed for as long as 8 hours after the infecting intraperitoneal injection. All the mice at this time have a septicæmia to the extent that there are several

hundred streptococci per 1 c.c. of blood. Successful treatment consists in giving fairly heavy doses of the drugs during the first 10 hours and then continuing with a single daily administration for at least six days. If the treatment is stopped before this time a number of the mice will die of the streptococcal infection. Mice that have recovered through treatment possess no demonstrable immunity to the hæmolytic streptococcus.

As the virulence of the strains used for producing such experimental infections decreases so do the protective results. The lower the virulence, the larger is the number of streptococci that must be injected. Just how important this question of dosage is it is impossible to state, but it is very clear that experimental results are obtained only with highly virulent strains of hæmolytic streptococci.

Among the other varieties of streptococci two are worthy of mention, *S. viridans* and the anaerobic streptococci. An *in vivo* technique has not been worked out for these two species, but by means of *in vitro* tests it has been shown that a number of strains of *S. viridans* derived from cases of subacute bacterial endocarditis are as susceptible to bacteriostasis as the hæmolytic variety. Strains of similar origin but of the faecal type are completely resistant in *in vitro* tests.

We have, as yet, no experimental data of the effect of these drugs on the anaerobic streptococci which are the cause in some puerperal infections. While only a small number of cases have been treated, the results indicate that the anaerobic streptococci are apparently not affected by sulphanilamide.

Other microorganisms.—The meningococcus can be made virulent for mice by injecting it intraperitoneally with mucin. Even more striking results than those with hæmolytic streptococci have been obtained with the meningococcus, using this technique. Mice can be protected from a million lethal doses by often only one administration of sulphanilamide, provided the drug is given early. When treatment is delayed the results are poor.

The mouse results in typhoid infections have not been as striking. The same is true for staphylococcal infections, for, while the animals may survive a hundred lethal doses, septic abscesses persist in the liver and peritoneum. Very little *in vivo* work has been done with

staphylococci because the organism is not highly virulent for experimental animals. In pneumococcal infections in mice the results have been quite good, especially when treatment is combined with type specific antiserum. Experimental animals have been protected from lethal intraperitoneal injections of *Cl. Welchii* by sulphanilamide, but this type of infection is not comparable to gas gangrene in man. Negative results have been obtained in experimental syphilis, in avian malaria, and with trypanosomiasis in mice.

Experimentally, the viruses of poliomyelitis, herpes, lymphogranuloma inguinale, encephalitis, and influenza have not been affected by the drugs. The exception to these negative findings with virus has been lymphocytic choriomeningitis in mice. Good results follow treatment with prontosil but not with sulphanilamide. Recently Dochez and Stanetz have reported the successful treatment of canine distemper with sodium sulfanilyl sulfanilate.

Therapeutic results in spontaneous diseases in animals would impress one more than those in induced infections. The only evidence that we have on the effect of sulphanilamide relative to natural disease in experimental animals is that reported by Seastone. He isolated two strains of hæmolytic streptococci from a naturally occurring disease of guinea pigs. One of these was highly virulent, the animals dying of septicæmia in about five days' time; they could be saved by sulphanilamide. The other strain, after intradermal injection, localized in the lymph glands with chronic abscess formation; when animals injected with this strain were treated immediately no sign of the infection occurred. If treatment was delayed for five days so that the infection was established sulphanilamide had no effect on the course of the disease, and it progressed as in the controls. This observation is important in connection with infections in man, especially as Hofmann reported that prontosil could not be found in the contents of stabilized abscesses. It apparently does not readily pass through the abscess wall.

Experimentally, it has been impossible to study the effect of sulphanilamide upon gonococcal infection, through the lack of virulence of the organism. But on account of the experimental results with the closely related meningococcus, and because the gonococcus is equally susceptible to bacteriostasis *in vitro*, and as sul-

phanilamide is excreted in high concentration in the urine it was hoped that these drugs would prove of value in the treatment of gonorrhœa. There was thus very little experimental evidence for their use in such infections.

Bacteriostatic tests.—*In vitro* tests are carried out by adding sulphanilamide in a concentration of 1:10,000 to media, and comparing the amount of growth with control cultures. This concentration is approximately that which is obtained in the blood stream during adequate therapy. The bacteriostatic action of sulphanilamide for a large number of different microorganisms, including those that infect the urinary tract, has been demonstrated by this means. The bacteriostatic effect is not interfered with by the presence of serum or blood in the medium, which reduces or nullifies the action of most other chemical antiseptics. Further, the white blood and other body cells do not appear to be damaged by the sulphanilamide. The bacteria are not killed, their growth is merely retarded. It is perhaps worthy of note that all strains of hæmolytic streptococci are not equally affected by sulphanilamide *in vitro*, for the bacteriostatic action is often greater on some strains than on others.

One would be very loath to interpret these *in vitro* experiments as indicating that a clinical response to infections due to these microorganisms was to be expected. It is a far enough jump from the experimental animal to man without going back to the test tube, especially as very slight changes in culture media markedly affect bacterial growth curves.

Mode of action.—Most of the recent experimental work has been directed towards elucidating the mode of action of these drugs. Their curative effect might be through a direct action on the bacteria themselves, either by destruction, by inhibition of growth, by alteration of virulence, by neutralization of toxic substances, or by interference with capsule formation. On the other hand their effect might be not on the bacteria but on the normal defense mechanisms of the host, stimulating the leucocytes or reticulo-endothelial system to active phagocytosis or in other ways altering the type and character of the tissue response to the irritant.

It has been convincingly demonstrated that sulphanilamide has no bactericidal action on the hæmolytic streptococcus. While there is some evidence of capsular or other membrane change,

radical alterations in the characteristics of mouse-virulent streptococci are not brought about by treatment with sulphanilamide. The only demonstrable action is retardation of early growth. These facts clearly point to the necessity of an adjuvant action on the part of the body fluids or cells. Such a possibility was considered from the very beginning of the experimental studies, for Domagk, noting an increase of mononuclear cells in the peritoneal exudate of treated mice, thought that the reticulo-endothelial system might play a fundamental rôle in the action of the drug. Blockade of the reticulo-endothelial system and splenectomy do not decrease the chemo-therapeutic action.

In experimental hæmolytic streptococcal infections both the leucocytes and macrophages are important defense cells. Mice die of an induced hæmolytic streptococcal infection despite adequate sulphanilamide therapy if the leucocytes are reduced by benzene to 500 per c.mm. In normal mice, however, sulphanilamide apparently produces a bacteriostasis sufficiently marked to protect the leucocytes and to allow the natural defense macrophages to accumulate. The drug itself does not stimulate the mobilization of the macrophages. Long has shown in experimental Welch bacillus infection of the peritoneal cavity that bacteriostasis due to sulphanilamide plays a determining rôle. While these experiments indicate that the bacteriostatic action of sulphanilamide plays an important part in the therapeutic result it is by no means certain that this is the full explanation, as other

possible modes of action have still to be investigated.

Recently a number of new chemical compounds have been found to be effective in experimental infections. The chemical structure of some of these is very interesting and throws much doubt on the importance of sulphanilamide and the sulphonamide configuration in effective compounds. We thus have a number of chemicals of very different structure that are effective in experimental infections, but we know very little about the value of any of them in infections of man. Sulphur in various functional states, as sulphonamide, sulphonate, sulphone, or sulphide, appears as a common constituent of all and is included as a radical in many of the derivative compounds. Although the benzene ring is found in most of the compounds the pyridine nucleus occurs in others.

The number of new drugs shown to be of equal or even greater value than sulphanilamide in animal experiments is increasing almost weekly, and if this continues the situation may indeed become chaotic. Adequate clinical trials have been conducted principally with sulphanilamide, but with so many compounds available a real problem confronts clinicians, to determine which of these may be most useful in human infections. The future holds hope that more effective and less toxic compounds will be found.

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THE USE OF SULPHANILAMIDE IN CLINICAL MEDICINE*

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THE employment of chemical substances as antibacterial agents has been a goal of medical science since the days of Pasteur, but the anticipation that chemical antidotes would speedily be found effective in combating bacterial diseases has not in general been realized. The apparently rational use of carbolic acid on the surface of the body soon led to appalling results and the discontinuance of this direct attack. It became almost axiomatic that the

undoubted potency *in vitro* of bactericidal chemicals could not be reproduced *in vivo* without endangering the lives of both tissues and host. Thus was ushered in the new era in which great advances were made in the knowledge of the so-called "immunity mechanism" of living animals. Even the triumphant discoveries of Ehrlich of the power of chemicals in combating non-bacterial organisms and the use of quinine in malaria failed to divert attention from the newer biological attack on microbial diseases. Despite the swing of the pendulum and the disappointments of the past there have always

* One of the papers in a symposium before the Section of Medicine, Academy of Medicine, Toronto, January 11, 1938, revised to date of May 15th.

been workers who fought for that earlier conception. Sulphanilamide and its derivatives are the result of this zealous striving. The extraordinary interest which is evinced in the drugs of this series is attested by the appearance in the literature of almost three hundred articles in the past thirty months.

In clinical practice the results of its use are not easy to assess. There are several reasons for this, but three in particular seem to be important. First, the time has been too short, secondly, the drug has been used in a multitude of diseases and in too many instances in a decidedly uncontrolled manner; thirdly, there has been considerable variation in the drugs and dosages employed, and many observers have neglected to use methods designed to determine the amount of active drug in the blood, urine and tissues of their patients. Therefore, an analysis of the literature on the clinical use of sulphanilamide warrants only general conclusions.

In the course of this presentation the word sulphanilamide will be used to include its protosil derivatives since their action is supposed to depend upon the elaboration of the simpler substance. It is beyond the scope of this paper to delineate the avenues of fresh researches which are bringing new and sometimes little related chemical substances into prominence. It is quite possible that one of these, or one yet to be discovered, will prove to be far more efficacious as a therapeutic agent than sulphanilamide; but sulphanilamide and its derivatives still hold the stage because their worth has been shown by both laboratory and clinical observation.

When any new remedy is brought to the attention of the medical profession three questions should be asked: first, what can it do to combat disease? secondly, what doses and in what form should it be given? thirdly, what harm may follow the therapeutic use of the drug in the prescribed doses?

What can sulphanilamide or its derivatives do to combat disease? Although there was some sporadic clinical use of these drugs before the publication of Domagk's paper, yet it is being found that the most spectacular results at the bed side have been obtained in conditions in which the responsible organisms have been shown experimentally to be most subject to the influence of sulphanilamide. It has been demon-

strated that almost all strains of beta-hæmolytic streptococci, with the notable exception of group D. (Lancefield), respond by experimental test to these drugs. Long has in fact suggested that a simple bacteriostatic test should be used as an indicator for the employment of sulphanilamide in any given clinical case.

Apart from puerperal fever no very large series of cases of hæmolytic streptococcal septicæmia are reported. If the results of Mitchell and Trachsler, Carey and Keefer are taken together there is a total of 18 cases (7 of whom were infants) treated with sulphanilamide, with recorded recoveries in 15, a mortality rate of about 17 per cent. A larger and more instructive series is that from Queen Charlotte's Hospital, London, as reported by Colebrook and his colleagues, and by Gibberd. Gibberd reported a death rate in puerperal fever of 20 per cent in 210 cases treated in 1934-5 by methods other than sulphanilamide, as against 4.5 per cent in 157 cases treated by this drug in 1936 and the first quarter of 1937. It has been argued that Colebrook and Kenny's earlier figures might possibly be explained by a startling alteration in virulence of the hæmolytic streptococci. When, however, in a more recent communication Colebrook and Purdie reported that of 199 cases treated by sulphanilamide the death rate was only 5.5 per cent as compared with an average death rate of 22.8 per cent for the previous five years there is some justification for their conclusion that it is, to use their term, "highly probable" that this improvement has been in an important degree due to the employment of sulphanilamide. Even more arresting are the results of this therapy in what Gibberd has termed the "invasive" cases, that is, cases of puerperal fever where the infective agent has spread beyond the birth canal and appeared in the blood. In 22 cases with positive blood cultures treated by chemotherapy Colebrook records the death of only 6 patients, a mortality rate of 27.3 per cent. These results stand in great contrast to those obtained in the four preceding years, 1932-1935, during which time there were 82 cases (untreated by sulphanilamide) and of these 52 died. The mortality rates for this group ranged in the various years from 58 to 93 per cent, with an average death rate of 71 per cent.

These statistics are highly encouraging, but for truly spectacular results it is necessary to examine the findings in cases of streptococcal meningitis. In a 35-year period (1901-1934) Gray reported that only 66 instances of recovery were to be found in the literature. More recently Trachsler *et al.* have been able by diligent search to add a further 23 recorded recoveries to this list, making a total of 89 cures in the pre-sulphanilamide era. The mortality rate of this disease was until 1935 accepted by competent observers as lying between 97 and 99 per cent of all cases. A cursory review of the recent literature shows that to date (a period of 30 months of sulphanilamide therapy) at least 56 recoveries have been recorded and that the recovery rate has, contemporaneously with the use of sulphanilamide, risen from between 1 to 3 per cent to 80 per cent in this disease.

In the treatment of erysipelas there is also general agreement that chemotherapy is very valuable. In this disease, except when it attacks infants, the debilitated or the aged, recovery is usually to be expected. The system of alternate or group controls is here particularly applicable. When this has been done it is found in series running into hundreds that the chemically treated cases show benefits *not approached by any other treatment* with respect to the rapidity with which the spread is arrested, the duration of the primary toxæmia and fever, the percentage of complications and the number of days the patients were required to remain in hospital. Most observers now agree that with adequate dosage of sulphanilamide the spread of erysipelas can almost always be arrested in within 16 to 48 hours after treatment is commenced.

In scarlet fever, by contrast, almost no good results have yet been recorded. There is some evidence, however, that the exhibition of sulphanilamide along with serum materially reduces the percentage of septic complications.

In streptococcal pneumonia there is not yet enough evidence at hand to warrant definite conclusions, although there are scattered reports of good results, especially in the treatment of empyemata in conjunction with aspiration or other forms of drainage. The results in streptococcal peritonitis are not encouraging. The same may be said of suppurative streptococcal abscesses and adenitis.

On the other hand there has been a general inclination to view with hope the effect of sulphanilamide and its derivatives in streptococcal otitis media and mastoiditis, and, with enthusiasm, its employment in tonsillitis and pharyngitis due to these organisms. It is, however, noteworthy that no great success has attended attempts to remove the streptococcus from carriers after scarlet fever, and some have warned that the treatment may actually increase the number of these.

The treatment of rheumatic fever, chorea, rheumatoid arthritis and other diseases of allegedly streptococcal origin has been devoid of good results. To date there are also no recorded recoveries in cases of streptococcal endocarditis, whether due to the hæmolytic or the *S. viridans*. Most anaerobic streptococci and the *S. faecalis* appear to be resistant to the drugs of this series.

In meningococcal meningitis there seems to be clear evidence that sulphanilamide is at least as effective as the antisera, but many clinicians believe that the combined treatment, where possible, should still be adopted. Schwenker reported 15 per cent mortality in 52 drug-treated cases against 30 per cent mortality in the serum-treated cases in the same epidemic in the same hospital. Although successes have been reported with the use of sulphanilamide by mouth or prontosil intramuscularly in meningitis there are many who think that this should be supplemented by intrathecal injections of 0.8 per cent sulphanilamide solution.

Sulphanilamide is, of course, being very widely used in the treatment of gonorrhœa, whether acute or chronic. Five authors recently reporting on several hundred cases *in toto* agree that with adequate and carefully supervised dosage from 70 to 90 per cent may be cured. There are many who believe these figures to be too high. Certainly the best results have been obtained with doses which are potentially toxic and when the treatment has been carried on for 2 to 3 weeks after apparent cure. Several have sounded a warning against a possible or actual spread of the disease by those who have deemed themselves cured after a few days' treatment. Gonococcal arthritis in the hands of some has been rapidly cured. Others have not had good results in this or in iridocyclitis.

In pneumococcal infections there is reason to hope that the drugs of this group may prove

to be of aid in some types. Attention is particularly being directed to type III in view of the characteristics of this organism and the encouraging nature of experimental data. Heintzelman Hadley⁷ and Mellon gave sulphanilamide in 9 cases of type III pneumonia and 7 recovered. In a control series of 10 cases there were 8 deaths. Figures are also given of a death rate of 75 per cent in 33 untreated cases in Pittsburg, as against 22 per cent in the treated group.

Dr. Harold Kinsey and myself have been using these preparations with what would seem to be a measure of success at the Toronto Western Hospital in type III pneumonia. In view of the commonly accepted high mortality rate in this infection our results of 5 cures in 5 treated cases, 3 of which had positive blood cultures, would seem at once to be decisive. There is, however, evidence that in the present season the type III pneumococcus infections are of a particularly non-lethal character, and for this reason the results to date are being considered tentatively. In two other cases in which sulphanilamide had no apparent immediate effect on the course of the disease it was found that the particular organism (type III pneumococcus) was insensitive to sulphanilamide by the *in vitro* bacteriostatic test, and treatment was therefore stopped. At the same hospital Dr. William Keith has kindly permitted me to see the records of an as yet unpublished case of type III pneumococcal meningitis in which under chemotherapy a complete and rapid recovery ensued. The pneumococcus was, in this instance, typed directly from the spinal fluid before treatment was commenced. Recently, a second cure in pneumococcal meningitis has been reported.

Very encouraging reports have appeared from the drug treatment of the *Cl. Welchii* infection in wounds. To add to the complexity of the whole question there is a recent report that in 100 cases of malaria (*vivax* and *falciparum*) dramatic cures have resulted in every case. There have also been reports on the good results of treating *Br. abortus* and *mellitensis* infections by the prontosils; and some cases of staphylococcal infections, even including septicæmia, have been unexpectedly improved.

Long and Bliss state that practically all the organisms found in the human urinary tract, with the exception of the *S. faecalis* are sus-

ceptible to the sterilizing powers of sulphanilamide in concentrations of 200 mg. of the free sulphanilamide in the urine. These organisms include, among others, the staphylococci, the coli, *B. proteus*, *Aerobacter aerogenes*, and the typhoid group. Clinical experience when it has rested upon systematic and adequate dosage has confirmed these results and established sulphanilamide as the most important anti-infective agent yet evolved for the treatment of urinary infections.

Summing up.—The drugs of the sulphanilamide group are particularly potent in clinical use against: (1) certain diseases due to the beta-hæmolytic streptococci. The more serious (or virulent) the disease, the more dramatic seem to be the results obtained. On the other hand in a considerable number of cases there have been unexpected failures, and this also applies to diseases due to other susceptible organisms; (2) the meningococcus, both in meningitis and bacteriæmia; (3) the gonococcus; (4) almost all organisms causing urinary infection; (5) *Cl. Welchii*; (6) malarial parasites (quartan particularly); (7) pneumococcus type III infections (some strains).

Results are questionable as yet with respect to staphylococcal infections, the typhoid group, and infections due to *Br. abortus* and *Br. mellitensis*.

Results are poor in certain diseases presumably caused by the hæmolytic streptococci, e.g., acute rheumatic fever, peritonitis, scarlet fever, *S. faecalis* pyelitis; in diseases caused by the *S. viridans*, in tuberculosis and most pneumococcal and influenzal conditions.

DOSE AND MANAGEMENT

Long and Bliss have reached the conclusion that since a 1/10,000 concentration of sulphanilamide (i.e., 10 mg. per 100 c.c.) was decidedly bacteriostatic to streptococci *in vitro* it is desirable that in severely ill patients, e.g., in septicæmia or meningitis, a concentration of between 1/10,000 and 1/7,000 of the drug in the blood should be attained. Marshall and his colleagues have been able by a simple biochemical method to estimate the concentrations of para-aminobenzenesulphonamide (sulphanilamide) in blood, urine, spinal fluids and exudates. Their researches have shown that sulphanilamide given by mouth is absorbed in about four hours and that a maximum concen-

tration in the blood is reached in four to six hours. Further, they showed that the drug is almost wholly excreted in the urine, and that with normal kidney function this takes place rapidly. It has been further shown that an approximate equilibrium is rapidly established in the concentrations of sulphanilamide in blood and body fluids and secretions in the normal person, a balance between intake and output of the drug being reached in 48 to 96 hours.

As a result of these important findings it is possible to establish a rational system of dosage in the human being. In the first place it is *obvious that by suitably dividing the doses a more or less uniform concentration may be attained*. Usually, therefore, doses are best administered every four to six hours. Secondly, by biochemical assay it is possible to determine whether, following oral administration, the optimal concentration of the drug in the blood (and therefore the tissues) or in the urine has been attained by the prescribed dosage. Lastly, the optimal concentrations having been attained, it is possible to determine whether it is being maintained, exceeded, or is falling off during the course of treatment. There can be no question that these are important facts to establish. At the Toronto Western Hospital, where, with the cooperation of Mr. Stewart Wilson, these methods have been in use since September, 1937, instances have been found where the drug given by mouth has not been absorbed into the blood stream in amounts commensurate with the dosage. In such cases good results cannot be expected unless this deficiency is overcome by suitable means. In other patients (notably those with pneumonia) an accumulation of the drug has been found to an amount of over 29 mg. per cent, or nearly thrice the optimal concentration, with doses which normally never produce anything approaching this figure. Failure to recognize this state of affairs quickly might well be expected to result in dangerous sequelæ. The suggestions of Long and Bliss have therefore been adopted, and in patients who are dangerously ill and who, therefore, are receiving heavy initial dosage it is the practice to estimate the blood concentration 4 to 6 hours after the heavy initial dose, to determine the level attained, and again at the end of 24 to 48 and 60 to 72 hours, to see whether it is being

maintained. This seems to be a rational procedure in the present state of our knowledge.

These remarks apply only to cases receiving sulphanilamide by mouth. When derivatives such as prontosil solution, etc., are being given, biochemical assay is not so easily applicable. It follows also that under these conditions, *i.e.*, parenteral administration, such methods are not so necessary, for in these circumstances the patient is at least sure to receive the total amount of the drug prescribed.

In general it has been found that in adults the administration of sulphanilamide in doses of from 3 to 6 grams per diem (45 to 90 grains) the blood concentration usually ranges between 2 to 6 mg. per cent, and with doses of 8 to 12 grams (120 to 180 grains) in 24 hours a level of between 8 and 14 mg. per cent is attained. It should, however, be stressed again that much higher concentrations than this have on occasions resulted from doses of about 100 grains a day in our experience.

Potentially lethal infections call for bold measures. Patients who are ill with very severe infections such as hæmolytic streptococcal meningitis, peritonitis, septicæmia, severe erysipelas, or meningococcal meningitis and bacteriæmia have a very poor prognosis. It is recommended that in such circumstances the possibility of the toxic effects of the drug should not deter the physician. It should be his aim to ensure that the patient receives in as short a time as possible a dose of sulphanilamide sufficient to raise the blood concentration to between 10 to 15 mg. per cent. The initial dose under these conditions should be in the neighbourhood of from 3.3 to 6.6 grams (50 to 90 grains) for an adult of 100 lbs. or more. Four to six hours later the concentration of sulphanilamide in the blood should be about 10 mg. per cent. To maintain that level 20 to 25 grains or 1.3 to 1.6 grams should be given every four hours until definite clinical improvement is observed, when the dose should be rapidly reduced, first by one-third, and then to one-third of the original amount. Finally, such a patient should receive about 3 grams or (40 grains) in divided doses (each of 10 grains) every six hours for ten days to two weeks, for it has been established that too rapid withdrawal of the drug sometimes results in uncontrollable relapses.

The above procedures are subject to modification according to the severity of the infection,

the weight of the patient, the fluid intake and the appearance of dangerous toxic manifestations. The papers of Long and Bliss or Carey may be consulted for greater detail in the grading of doses for children and infants.

When, as not infrequently is the case, either oral administration is impossible, or absorption is found by biochemical assay to be inadequate, recourse must be had to parenteral administration. The cheapest, and in some respects the most desirable, method is the use of a 0.8 per cent of sulphanilamide in physiological saline. This can be made up by the physician. Simpler, but more expensive, is the use of prontosis solution. If this is used it is necessary to bear in mind that a 5 per cent strength is coming on the market, and the amounts advocated in the literature refer to the 2.5 per cent solutions. These substances are injected subcutaneously or intramuscularly. They may be used to supplement oral administration of sulphanilamide or to supplant it. Full details of administration may be found in the papers of Long and Bliss, Carey or Colebrook.

So much for the treatment of fulminating infections. *In milder infections, whether streptococcal or not, it is certainly wise to avoid a heavy initial dose and gradually to work up to a blood concentration of 5 to 6 mg. per cent over a period of one to two days.* In this way idiosyncrasies to the drug may be detected before unnecessary harm is done.

In estimations of the concentration of sulphanilamide, whether in blood or urine, it is found that part (in the blood, usually only about 10 to 20 per cent, whereas in the urine the values vary between 33 and 66 per cent) of the total sulphanilamide is bound or conjugated. It is thought that this conjugation is due to the formation of an acetylated form of sulphanilamide. By most observers the conjugated sulphanilamide is considered to be relatively ineffective in combating infection. The remainder is termed the "free" sulphanilamide. This discovery has an importance in the treatment of urinary infections, for it is recommended that the dosage should be such that between 75 and 100 mg. per cent of free sulphanilamide should be present in the urine in order that optimal conditions should prevail. Occasionally it may be necessary to employ concentrations as high as 250 mg. per cent. As the normal kidney has great concentrating power with respect to

sulphanilamide it is not necessary to give large doses to attain this figure. It naturally follows that less of the drug will be required if the fluid intake is not excessive. For this reason the intake of fluid is best given in divided doses and maintained between 1,200 and 1,400 c.c. in 24 hours in the treatment of urinary infections.

TOXIC MANIFESTATIONS

It is desirable to consider the toxic manifestations under two heads: (1) those which are common and seldom severe enough to cause alarm; and (2) those which are rare but dangerous and contraindicate continuance of treatment by sulphanilamide.

Under the first group are malaise, giddiness, tinnitus and a feeling simulating alcoholic intoxication, depression, gastro-intestinal irritation, anorexia and nausea. These effects are much more common if the patient is ambulatory and seldom are severe if he is confined to bed. Almost all patients on moderately heavy doses of sulphanilamide show a fall in the CO_2 combining power of the blood. This is attributed by some (Long and Bliss and Southworth) to acidosis and it is recommended that 10 grains of sodium bicarbonate be given with every dose of sulphanilamide.

Some degree of cyanosis has in various series been found to occur in as many as 80 per cent of the cases treated. It seems to be more severe with heavier doses but this is not invariable. It appears to be due to three different conditions. Marshall and Walzl have found that it may be due to a black oxidation product of sulphanilamide which has been called "aniline black". Certainly, almost as common is the cyanosis caused by the formation of methæmoglobinæmia. In the presence of sulphur or sulphur-compounds this may result in the production of sulphæmoglobin. None of the cyanotic manifestations are contraindications to continued treatment unless they result in a serious depletion of the oxygen-carrying capacity of the blood, but the appearance of more than a mild degree of sulphæmoglobinæmia is wisely viewed with concern. In addition, a marked increase in any of the mild symptoms especially when diarrhoea, abdominal pain, tingling of the hands, tachycardia, dyspnoea, and pain in the chest occur are danger signs and at least call for an interruption of treatment.

In the second group the following toxic effects are serious enough to warrant immediate withdrawal of the drug.

1. Fever, seldom appearing before the third to fourth day, usually between seven to ten days. Treatment may sometimes be recommenced in smaller doses after 48 hours withdrawal; but fever is a signal of dangerous import. In febrile patients confusion may exist as to the origin of the fever but an unexplained sudden rise in temperature during the course of chemotherapy, especially if accompanied by a rash or other evidences of toxicity, is likely to be due to the drug.

2. Morbilliform and maculopapular, or even vesicular rashes seldom occurring before the third day. There seems to be quite definite evidence that exposure to ultra-violet light or sunlight is in many instances the precipitating cause of their appearance. Such exposure should be avoided. A few cases have been reported of dermatitis of the exfoliative and other types occurring during treatment. There are also suggestions that in rare instances patients may exhibit an extreme sensitivity to sulphanilamide which amounts to an allergic response. All the above toxic effects, except the severe dermatitides, disappear within 48 to 60 hours after cessation of dosage. Many of them may be avoided if the fluid intake can be kept high; and the most effective way to rid the body quickly of the drug when such effects have been produced is to administer excessive fluid.

3. The occurrence of sulphæmoglobinæmia is another indication for the termination of treatment unless it is only moderate in degree. On theoretical grounds sulphur in any form, whether as sulphates or sulphides, should never be given in any combination during the course of sulphanilamide therapy. There is good evidence that substances like ferrous sulphate or magnesium sulphate, given in the three days preceding the commencement of treatment, may have deleterious effects in the period of treatment. It is also desirable that no cathartics which cause liquid stools (and therefore favour the formation of hydrogen sulphide in the bowel) should be permitted. The safer method is to depend on enemata or inert oils (paraffin), although cascara has been used without untoward results. It is good practice to administer an enema before treatment is begun.

It is unwise, in fact, to use any drug whatsoever (with the exception of sodium bicarbonate) during treatment, and particularly to eschew phenacetin, acetanilide, methylacetanilide and any drug related to aniline or nitrobenzene. In the diet eggs and onions should be omitted or restricted to one or two per day. Sulphæmoglobin may require six weeks for its complete disappearance. When severe depletion of the oxygen-carrying power of the blood has occurred transfusions may be required as emergency measures.

4. The most serious toxic effects of the drug relate to the blood. Possibly because they contain a benzene ring, sulphanilamide and related compounds have certainly been responsible for damage to the bone marrow. Instances have been recorded in which a rapid drop in hæmoglobin and red blood corpuscles has occurred associated with hæmolytic icterus. In most of these the immediate withdrawal of the drug leads to a complete recovery within a week. In other cases blood transfusions have been employed as emergency measures. There have also been at least five deaths from agranulocytosis, and several observers have reported significant and even alarming falls in the white blood count. All patients on sulphanilamide therapy should have repeated blood examinations; and *with heavy dosage these should be done daily as a routine.*

5. Three cases of optic neuritis have been reported.

It will be clear from this review that patients on moderate or heavy dosage should be confined to bed, preferably in a hospital where the necessary facilities are available to detect and treat toxic manifestations as they arise.

Two independent workers have recently proved that there is an increase in porphyrin in the urine in patients exhibiting toxic reactions to sulphanilamide. Pointing out the close similarity between the milder constitutional symptoms after sulphanilamide and those found in acute porphyrinuria, they suggest that estimations of the urine for porphyrin may prove to be an early guide to the imminence of severe toxic effects.

This paper would be incomplete without some reference to the sulphanilamide-Massengill catatrophe which for a time cast unmerited criticism on the prontosils. Although the American Medical Association and the collaborating authorities have completely exonerated sulphanilamide from

having played any part in the causation of the 73 reported deaths resulting from the use of the Massengill preparation, yet there is ample evidence that the drug and its derivatives are in themselves compounds of considerable toxicity for some persons.

In conclusion, there can be no doubt that this form of chemotherapy constitutes a great advance in the treatment of some diseases. It is also evident that these drugs are very toxic and should only be employed under the closest medical supervision. The Ontario Medical Association and the provincial authorities are to be congratulated on the Order in Council of

January 6, 1938, by which sulphanilamide and its derivatives were placed on the restricted list.

Some sixty references were quoted in this paper, but since it was read comprehensive bibliographies have appeared in the literature. The author has therefore suggested that the following papers be consulted as key references.—[Ed.]

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A PRELIMINARY REPORT ON SULPHANILAMIDE AS A URINARY ANTISEPTIC*

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THIS paper deals simply with the present status of sulphanilamide. Innumerable problems present themselves that will require investigation, and at present we can speak with certainty about only a few phases of its use. Probably we know more of the clinical than any other phase, but certainly we are at the beginning of a new chapter in therapy. Other compounds will undoubtedly appear. Some of these compounds may be improvements; some may be less toxic; some may be more efficacious, but it will be difficult to assess these new developments if the facts about the present drug are not learned and carefully recorded. The more one studies sulphanilamide and its effects, the more complicated the study seems, and it is becoming more apparent how necessary controlled observation is for the successful, intelligent, and safe administration of the drug. This is truer of general conditions than of urological, but it is very true of the latter also.

It has been the good fortune of urologists who deal in visible and tangible infective conditions to find in this drug an agent whose action is not only visible to the eye but which can be checked by chemical and bacteriological examination. In other words where the physi-

cian must rely in most instances on experience to determine the effect of the drug on his patient the urologist has many simple methods of estimating its efficacy. We in urology are not so concerned with blood concentration of the drug, although we do not lose sight of lurking dangers, but we are concerned with its urinary concentration, the control of the urinary acidity, the elimination of the drug and in what form at the kidney.

After administration sulphanilamide has been recovered from all organs and all body fluids satisfactorily except the faeces and bile; that it is present in these situations is likely, but chemical recognition has not as yet been wholly successful. It has also been determined that sulphanilamide is present, wherever found, both in the free state and also conjugated, in part at least as an acetyl derivative. The degree of conjugation varies in different individuals and in animals. Why conjugation occurs is a matter of conjecture. It has been suggested that it is a defence effort by the individual to whom the drug is toxic. As the drug is definitely less toxic to some than to others this could well be the case, and so far our results show a trend to increasing conjugation with increasing toxicity. There is great variation in the percentage of conjugated drug in the blood but the urine always shows an increased percentage of it:

* One of the papers in a symposium before the Section of Medicine, Academy of Medicine, Toronto, January 11, 1938.

where, why, and how this conjugation occurs is still a mystery, so far of little significance and probably actually of little importance, any more than how or why the drug acts as long as it does act with beneficial results. As to the relative merits of the free and conjugated drug as antiseptics, opinion varies.

Sulphanilamide was first used in urology for the treatment of Neisserian infection, and was heralded with many extravagant notices; one of the first was a claim of curing all cases in four days by the use of 16 five-grain pills. However, time has reduced its use and the expectancy of cure in this field to a reasonably stable level on a fairly definite routine dosage. This has been reported before, but a short summary of this aspect of the drug therapy is given.

The conclusions to be drawn from the work reported in this paper are:

1. That sulphanilamide has a specific action on gonorrhœal infection, both acute and chronic, and that it will cure these patients in about 30 per cent of cases, given cooperation.
2. It reduces the pain, discomfort and discharge associated with the disease in about 80 per cent of cases.
3. It reduces and almost eradicates the possibility of complication so frequently associated with the disease as we have known it.
4. It has little effect on non-specific urethritis. Some cases are benefited but the majority are not.
5. The drug is undoubtedly toxic to some patients, but the manifestations have not in this series been of a serious nature.
6. A small percentage of patients suffering from specific urethritis show no benefit from the use of sulphanilamide.
7. Sulphanilamide frequently cures the specific infection and leaves the co-existing non-specific infection unimproved.
8. Sulphanilamide cannot be given along with arsenical treatment.

Investigation with a view to determining why some patients show no response to sulphanilamide is negative so far. Further work is planned in regard to the possibility of different types of conjugation of the drug in different individuals.

Sulphanilamide is being used extensively by us in the treatment of routine urinary infections, probably much more frequently than is generally known, and it appears to be more

active in the upper portions of the urinary tract than in the urethra; not only is the dosage required smaller, but also we can regulate its concentration in the urine to what at present is considered at least sufficient to produce effectively antiseptic urine. That this minimal effective concentration is optimal is still undetermined; we are beginning to explore the realms of greater concentrations. We can concentrate the drug in the urine in two ways, by decreasing fluid output and by increasing the intake of the drug. Effective bactericidal concentration is probably not under 100 mg. of total combined and uncombined drug per 100 c.c. of urine. This concentration is not easy to obtain on a daily dosage of 30 grains until the body has been saturated, and as some fail to reach the desired levels on this dosage some check is necessary in those patients where treatment has apparently failed. Moreover, there are a great many factors affecting the action of the drug, and these will be discussed briefly. The first and most important consideration is the pH of the urine. The drug is weakly bacterostatic in acid urines but increasingly bacterostatic with increasing alkalinity, so that an infected urine made markedly alkaline becomes sterile, whereas the same urine allowed to remain acid remains infected. The proof of this is shown by experiments *in vitro*. Clinically, this is proved by patients who developed what was considered minimal sufficient sulphanilamide in acid or neutral urines to be efficacious, but showed no improvement. These urines became clear on the same concentration of sulphanilamide in the urine, once the urine was made alkaline. Of course, to really know that the patient is excreting sufficient sulphanilamide in the urine is important. Many cases have been treated on a routine dosage and regarded as failures in treatment, but later investigation showed that these patients had very little of the drug in the urine. Increased dosage resulted in increased urinary concentration of the drug with improvement of the urinary infection.

The organisms infecting the urinary passages have been classified and re-classified, and at each re-classification more and more organisms are reported as having yielded to sulphanilamide therapy, and it would seem that probably all organisms commonly found in the urinary tract, other than tubercle bacilli, will respond eventually. This is true of the routine case.

but we still cannot claim that all patients will respond even with an adequate dose. There are those who will respond and there are still those who will not, but certainly some types of urinary infection are responding to sulphanilamide that never before responded to drug therapy.

The patients treated by sulphanilamide and given adequate controlled dosage can be divided into three classes: (1) those whose urines are cleared and cure established as proved by stopping the drug without return of the infection; (2) those who are apparently cured but whose infection returns immediately the sulphanilamide disappears from the urine; (3) those who for some reason or other do not respond at all.

The group that responds to give complete cure needs little consideration. But the group with response and relapse is a distinct problem, and unfortunately this is a big group. Is it that there is a focus somewhere that has not been properly eliminated? Such would seem to be the only answer. How long may the drug be continued without damaging the patient's other systems? These are the problems to which the answer is as yet unknown. It would seem that the patient whose urine fails to stay clear should be given an extremely careful urological examination to disclose the source or cause of the recurring pyuria. A chronically infected prostate or vesicle could well be the origin of the infection. The drug has been given over long periods of time, but we are coming to the belief that if properly applied and not visibly effective in 72 to 96 hours, provided satisfactory urine or blood levels have been reached, it will likely fail completely in its purpose. A patient who has responded favourably and then has suffered a recurrence frequently requires heavier dosage, or even fails to come under control a second time, although the same infecting organism is present and there has been no known change in the patient.

Saturation of the body must occur before sulphanilamide appears in good concentration in the urine. The dosage usually applied is 30 grains on the first day, 40 on the second, 60 on the third, then a decrease to 30 grains daily, and the dosage is maintained at this level, while the urine output should be restricted to 1,200 to 1,500 c.c. daily. The initial small dose is given to test the patient as to toxicity, and the increase in the succeeding two days is to saturate the body and raise the urinary output to satis-

factory levels. Once the body has been saturated, the daily dosage of 30 grains maintains an adequate output of the drug, which, if the urine output is controlled, is well within bacterostatic limits. This limit was originally considered to be 25 to 75 mg. per 100 c.c. of urine, but very few of our urinary infections have responded to less than 100 mg. per 100 c.c. of urine. However, once the infection has been cleared, concentrations below 100 mg. per 100 c.c. seem sufficient to prevent recurrence of the pyuria. Urines once cleared have stayed clear on urinary concentrations as low as 35 mg. per 100 c.c. of sulphanilamide, and this concentration can be maintained on 20 grains daily with the usual check on fluid intake.

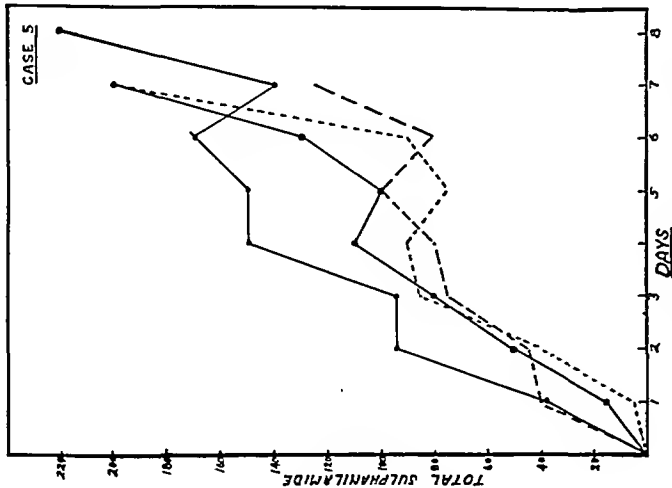
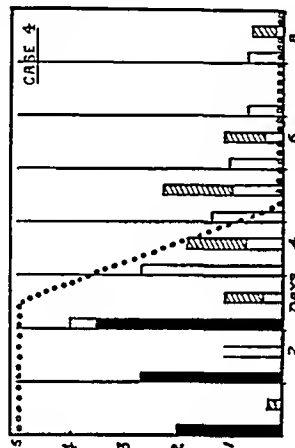
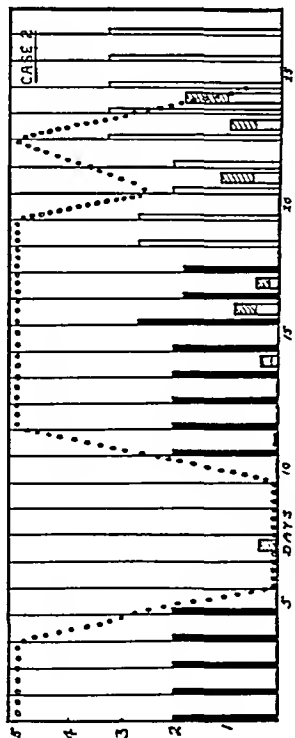
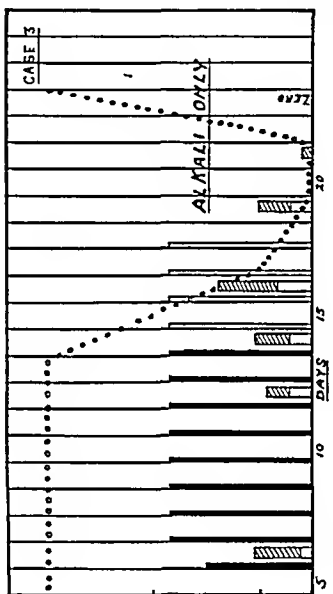
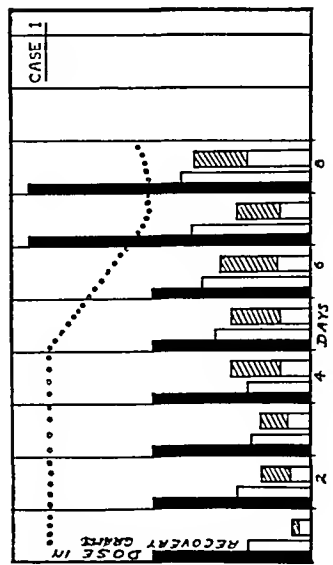
All patients do not follow a definite rate of saturation and excretion of the drug. Some reach satisfactory levels in two days, while others take three or four or even five days. Why some patients have delayed output in the urine is not understood.

Once the patient has been saturated on a given dosage, the output of the drug in the urine is one-third to one-half of the intake by mouth. Where the rest of the drug goes we do not know. It is not being excessively piled up in the system for it disappears from the urine in three to four days after stopping the intake. Peculiarly enough, the drug eliminated towards the end is almost entirely in the conjugated form, in our cases. And as there is no return of the infection until practically all the conjugated drug has disappeared from the urine it is reasonable to suppose that the conjugated drug is active in combating infection.

If there is no response to minimal therapeutic concentration of the drug in urine that has been alkalinized increasing the concentration of the drug is often effective. One such effect was obtained in a patient of S7, whose chart is shown. The age factor is playing less and less part as a contraindication to this particular drug therapy. But one must realize that any such patient must be under close supervision, and an accurate check made to know when adequate dosage has been achieved or else the patient may be exposed to unnecessary risk.

The problem that requires considerable investigation and which concerns all infections of the urinary tract is to know when absolute cure has been achieved. Urine once made clear by means of other antiseptics, for example, hexa-

CHARTS



Case 1 (Chart 1).—The tall black lines represent the total daily dosage in grains.

The clear column beside the dosage column represents the total drug recovered in the same 24 hours' output of urine.

The shaded column represents the return of sulphanilamide in the urine in mg. per 100 c.c. of urine multiplied by 100. The lined portion of this column represents the conjugated drug, while the unlined portion represents the free portion.

The circles represent the number of pus cells per high power field. On the first six days the dosage was 15 grains daily, and not until the fourth day did the concentration of the drug reach minimal concentration. During the first four days the return of the drug was little (less than one-third of the intake) whereas after the fourth day it was almost one-half the intake, indicating saturation of the body and consequent increased output. The relative concentration of combined and free drug are about equal and it can be seen that the infection was improved when minimal concentration in the urine of a patient whose output averaged 1,200 c.c. daily.

Case 2 (Chart 2).—The black columns represent the daily dosage of sulphanilamide. The clear columns represent the daily dosage of sulphanilamide while alkalis were also being given. This chart shows: Response with clearing of the urine on five days' 30-grain dosage of sulphanilamide.

The urine still clear, with only conjugated drug remaining in the urine two days after cessation of the drug intake.

Prompt return of infection when the urine became free of sulphanilamide. Failure to bring the patient under control again on the original dosage of sulphanilamide.

The response when alkali is added, but return of infection on reduced dosage of sulphanilamide.

Increased dosage with alkali finally improves the infection, but ultimate failure to control the infection by sulphanilamide must be admitted.

Case 3 (Chart 3).—This chart shows no response to minimal sulphanilamide concentration in the urine. However on the same dosage plus alkali the urine is cleared. The sulphanilamide was discontinued, the alkali continued, and the infection returned as soon as the sulphanilamide disappeared from the urine, which suggests that the alkali simply activated the sulphanilamide present in the urine.

Case 4 (Chart 4).—This patient was considered a failure to sulphanilamide therapy on a previous occasion. He had been on a 30-grain dosage. This time he was given 30, 40, 60, 10, 30, 15, 15 grains on consecutive days, with alkali added at the end of the third day. The drug concentration became adequate, the infection disappeared, and has not returned on a daily dosage of 10 grains.

Case 5 (Chart 5).—This chart shows varying rates of concentration of sulphanilamide in different patients on the same dosage and the same urinary output. Two reached minimal concentration in four days, one in six, while one did not achieve minimal concentration until the drug intake was increased.

mine, usually remained sterile after discontinuing the drug, but this is not the case with sulphanilamide. The majority of our patients show a prompt return of the infection when the drug disappears from the urine. After this has happened four to five times one begins to wonder just how much good has been done the patient. Should we keep the patient on a small adequate dosage for a long period of time or should we revert to another well known antiseptic, mandelic acid, or even ammonium chloride and hexamine? Unfortunately, we have experienced practically the same embarrassing recurrences with mandelic acid, and the answer seems to lie with the urologist, to find a focus of infection.

As stated the drug is being used with increasing frequency in our clinic and is gaining some ascendancy over mandelic acid for several reasons, although this is not because it is any better urinary antiseptic. Speaking in a reverse manner, we can best illustrate the point by referring to the shortcomings of mandelic acid. First, as a therapeutic agent mandelic acid is difficult for many patients to assimilate; secondly,

it is essential that the urine have a marked acidity, the production of which is frequently impossible even with added acidifiers. The use of mandelic acid is contraindicated in the presence of kidney and liver damage. Also mandelic acid is expensive. On the other hand, sulphanilamide is easily assimilated, the urine can readily be made alkaline, and the drug is inexpensive. In a direct comparison with mandelic acid we have found that sulphanilamide fills some gaps that mandelic acid does not and never will fill; not only that, but it will accomplish practically everything that mandelic acid is able to do if it is properly applied. Still one is left with the impression that sulphanilamide perhaps achieves a quick temporary alleviation but does not effect a permanent cure. In its present form, therefore, it is not the perfect urinary antiseptic.

I wish to thank Dr. Pearce for his advice, assistance, and kindly criticism, and Sir Frederick Banting for making it possible to have the collaboration of the biochemical division of his department. The chemical work is being done with the assistance of Dr. C. C. Lucas, to whom I wish to express appreciation and thanks.

SILICOSIS: AN EXPERIMENTAL STUDY OF THE LEACHING OF SILICATES IN TISSUES

BY HELEN E. WILLIAMS AND D. A. IRWIN

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INTRODUCTION

THIS paper reports an experimental study of the solubility and change in composition of selected silicates and quartz following their injection into, and recovery from, the subcutaneous tissue of rabbits after one to six months. The purpose was to learn whether the selected silicates, when present in animal tissues, undergo any demonstrable change in their chemical composition, forming substances more toxic than the material used for injection.

It is now generally agreed that when retained in the lung free silica is the only siliceous material that is capable of producing a nodular pulmonary fibrosis. Silicates alone, with the exception of asbestos, are regarded by Sayers, Miller and Yant¹ and Haynes² as incapable of producing a similar response. Asbestos, a magnesium silicate, is known to be responsible for a diffuse rather than a nodular type of fibrosis.

Experimental evidence, such as that obtained by Beger,³ strongly suggests that the body fluids selectively remove the magnesium from asbestos fibres, leaving the silica free. For this reason asbestosis is not regarded as a silicosis but rather as an indirect silicosis. This viewpoint is also held by Cooke.⁴

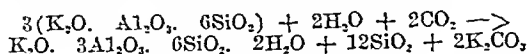
The question arises—may this idea of the selective removal of the basic constituents of the mineral be extended to other silicates? Beintker,⁵ Timmermans⁶ and Gerbis and Ueko⁷ have suggested that silicates are broken down into silicic acid in the tissues. Beger⁸ stated that the action of the dust is due to free silica, whether it contains quartz or silicates—meaning that in some manner the silicates must be decomposed before the damage is done. Koppenhoffer⁹ explained the phenomena by the fact that magnesium and iron are dissolved out and then replaced by alkalis, thus forming soluble silicates. Fowweather¹⁰ made the following

statement concerning the possibility of the leaching of silicates in the production of silicosis.

"If from the actual amount of ash and silica found in this case are subtracted the amounts found in normal lungs the differences are approximately the same (in 5 cases), i.e., the amount of ash in these lungs in excess of what would be present in normal lungs is wholly accounted for as silica. Yet the material inhaled in this case, viz., asbestos, was not free silica, but a complex silicate containing considerable amounts of other oxides besides that of silicon. One cannot avoid the conclusion that the asbestos has undergone decomposition in the lung, with deposition of SiO_2 , and removal of the metallic oxides. Herein is possibly the clue to the production of silicosis, namely, that it is due to the chemical action of silica, either inhaled in a chemically active form, or liberated *in situ* from inhaled silicates capable of relatively easy decomposition within the lungs."

Research, stimulated by Jones¹¹ theories concerning the importance of sericite, has laid still greater emphasis on the solvent action of lung-fluid and blood-lymph on selected silicates. Brammall and Leech¹² point out that the mineral residues stressed in medical reports on silicosis are silica, alumina, and ferric oxide almost exclusively, even in the cases where the inhaled dusts must have contained appreciable quantities of bases such as potash, soda, lime, magnesia, ferrous oxide, etc. They suggest that the residuals mentioned above are relics of antecedent mineral species which have been leached of their bases by biochemical processes. They compare the fate of the inhaled dust in the biochemical environment of the lung to the resulting products of weathering in nature, giving sericite, an intermediate product in the change of feldspar to kaolin, as an example.

Geologists have expressed the weathering phenomenon in the following equation:



It is seen that in the formation of sericite a large quantity of free silica is split off, and that its solubility would probably be considerably increased by the potassium carbonate, another product of the reaction. This reaction might take place in the lung and explain the finding of sericite in so many silicotic lungs and its failure to produce silicosis when inhaled or injected.

EXPERIMENTAL

The desired information was: (1) the possibility of any marked change in the composition of the dust, as shown by chemical analysis; (2) the relative solubility of the dusts, as shown by the percentage recovery from the tissues; and

(3) the tissue response produced by the presence of the injected materials.

Recent x-ray findings have shown quartz, microcline, orthoclase, oligoclase, albite, sericite and talc to be the minerals most commonly found in silicotic lungs.¹³ It was therefore decided to use this group of minerals in this investigation. Quartz was obtained in the form of optically clear rock crystal. The microcline, oligoclase, albite and orthoclase used were chosen for their purity by the Department of Mineralogy of the University of Toronto. Talc was procured from Madoc and was purified by means of gravity separation.* Sericite was separated in the same manner from Porcupine underground sericitic schist. As a control for the relative solubility determinations (percentage recovery), silicon was chosen, since it was considered an inert, insoluble dust. It was obtained from the American Carbide Company.

The above materials were all ground in ease-hardened steel ball-mills until all particles were less than five microns in diameter. They were then washed with 1:1 HCl and H_2O to remove any contaminating iron, and were dried at 110°C . The silica, aluminium and magnesium contents of the dusts were then determined. Silica was determined gravimetrically, aluminium was precipitated and weighed as the phosphate, and magnesium was precipitated by 8-hydroxyquinoline and determined volumetrically.

Suspensions of 1 g. of each of the finely particulate materials in 25 c.c. of water were obtained by adding a few steel ball bearings and approximately 5 mg. of a dispersing agent ("dispersaid") to the dusts in 50 c.c. Erlenmeyer flasks. To produce uniform suspensions of the dust it was necessary to add the water, a few c.c. at a time, with continuous swirling of the flask. These suspensions were injected subcutaneously into each of 75 rabbits, care being taken to spread the dust over a large area of the back. By rinsing the flask two or three times with distilled water very few milligrams were left behind.

One rabbit of each dust group was killed each month. The skin of the back was removed and digested in concentrated nitric acid. The dust was recovered from the acid and analyzed.

* Mixtures of tetrachlorethane (specific gravity 1.60) and tetrabromoethane (specific gravity 2.964) were used to prepare fluids of the required specific gravity for this fractionation.

TABLE

Column No. 1 Col. No. 2 Col. No. 3 Col. No. 4 Col. No. 5 Col. No. 6 Col. No. 7 Col. No. 8 Col. No. 9 Col. No. 10 Col. No. 11

Dust injected	Injection period in weeks	Percentage recovery of dust	Percentage silica in recovered material	Percentage silica in original material	Average difference in percentage SiO ₂ after recovery	Average difference in percentage SiO ₂ after HNO ₃ treatment alone	Percentage Al. in recovered material	Percentage Al. in original material	Average difference in Al. after recovery	Average difference in percentage Al. after HNO ₃ treatment alone
Albite Na ₂ O. Al ₂ O ₃ . 6 SiO ₂ .	1	88.0	69.0	65.5	+2.7	+2.4	10.3	9.9	+0.6	+0.5
	3	72.8	68.6				10.4			
	4	85.7	67.0				10.8			
	8	72.4	68.0				10.0			
	12	79.3	68.7				10.6			
	16	81.2	67.4				10.9			
	20	83.2	67.5				10.5			
	24			
Orthoclase K ₂ O. Al ₂ O ₃ . 6 SiO ₂ .	4	71.5	66.2	64.0	+2.0	+2.4	9.8	8.6	+1.6	+0.7
	7	52.2	65.8				9.8			
	12	75.5	65.7				9.4			
	16	65.2	65.0				12.2			
	16	71.8	66.8				10.0			
	20	78.4	66.6				10.3			
	24	86.2	65.6				9.9			
	24			
Microcline K ₂ O. Al ₂ O ₃ . 6 SiO ₂ .	3	77.0	66.9	65.3	+1.3	+2.3	9.1	8.8	+0.9	+0.7
	4	83.0	66.3				9.7			
	8	81.6	66.8				9.7			
	12	81.8	65.1				9.5			
	16	80.0	66.1				8.2			
	20	64.1	66.8				11.7			
	24	81.1	66.5				9.3			
	24	77.4	66.3				10.3			
Oligoclase 4 Na ₂ O. Al ₂ O ₃ . 6 SiO ₂ . 1 CaO. Al ₂ O ₃ . 2 SiO ₂ .	1	86.2	67.3	64.7	+2.0	+2.0	11.0	11.2	-0.4	+0.5
	5	85.3	67.1				11.5			
	7	59.7	67.3				10.5			
	7	90.2	67.1				11.3			
	12	79.5	67.0				10.4			
	16	77.0	67.0				10.5			
	20	70.0	65.0				9.6			
	24	73.3	66.3				11.4			
Sericite K ₂ O. 3 Al ₂ O ₃ . 6 SiO ₂ . 2 H ₂ O.	3	29.0	55.3	50.0	+5.8	+4.8	16.5	16.3	+0.6	+1.6
	4	44.4	55.0				16.5			
	8	45.4	55.0				18.3			
	12	45.6	57.7				16.9			
	16	48.5	55.0				16.0			
	16	46.9	53.8				17.6			
	20	66.0	59.7				16.0			
	24	69.7	55.0				17.1			
							Percentage mg. in recovered material	Percentage mg. in original material	Average difference in mg. after recovery	
Talc 3 MgO. 4 SiO ₂ . H ₂ O.	1	76.0	61.9	62.0	+3.0	+7.7	19.5	18.3	+0.5	
	1	87.0	68.4				16.4			
	4	67.4	64.5				18.4			
	8	76.6	63.0				19.4			
	12	72.9	65.0				19.0			
	16	75.7	63.7				18.8			
	16	77.3	68.4				20.2			
	20	79.2	61.0				19.5			
Quartz SiO ₂	3	83.0	99.8	98.2						
	4	85.3	98.6							
	8	74.8	99.2							
	12	75.6	99.5							
	16	81.7	98.0							
	24	74.1	99.3							
Silicon Si	1	86.0	96.4	98.8						
	4	86.0	98.5							
	8	87.0	96.6							
	12	68.6	96.6							
	16	59.0	97.9							
	20	55.0	97.5							
	24	64.4	99.1							
	24	52.0	96.3							

The results are given in columns Nos. 3, 4, 6, 8 and 10 in the accompanying table.

The effect of the nitric acid on the silicates was determined by treating one-gram samples of the dusts of known composition alone for the same length of time, then recovering and analyzing. The changes in the per cent silica and aluminium contents as a result of the nitric acid treatment are given in columns 7 and 11.

PATHOLOGICAL FINDINGS

Quartz produced its characteristic proliferative fibrosis. The injected areas showed a marked thickening up to the second month, after which firm nodules appeared.

The tissue response produced by the silicates and silicon contrasted sharply with that of quartz. These injected areas showed only a slight soft thickening. Slight differences in the degree of tissue response to these materials were noticed. Silicon produced the least reaction, sericite the most, while the others were intermediate and could not be distinguished from each other.

OBSERVATIONS

1. The amount of dust recovered from the skin bears no definite relationship to the length of time the dust was present in the tissues (with the exception of silicon). (Columns 2 and 3).

2. The recovery of silicon is less than that of quartz or the silicates (with the exception of sericite). (Column 3).

3. The recovery of sericite is considerably less than that of the other dusts. (Column 3).

4. The figures obtained for the percentage silica in the recovered materials are as constant as could be expected, the variations being well within the limits of the possible experimental error. The results for talc and sericite are not as constant as those found in the other materials. Possibly this may be explained by the fact that they are the only two minerals having water of crystallization. (Columns 4 and 1).

5. There is an average increase in the percentage silica in the recovered materials of 2.8 per cent in all the silicates. It is noted that sericite is again outstanding—showing a difference considerably greater than the average (5.8 per cent). (Column 6).

6. The aluminium content shows a slight increase in most of the dusts, but not a significant change—an average of 0.8 per cent. (Column 10).

7. The magnesium content of the talc shows also a slight, but insignificant increase (0.5 per cent). (Column 10).

8. The nitric acid treatment alone results in an average increase in the silica content of 3.6 per cent and in the aluminium content of 0.8 per cent in all the silicates. Here talc shows the greatest change (7.7 per cent). (Columns 7 and 11).

DISCUSSION OF OBSERVATIONS

Percentage recovery of dusts.—

(a) *General.*—The average recovery of oligoclase, microcline, albite, talc and quartz was approximately 80 per cent. Orthoclase and silicon were recovered to the extent of 70 per cent and sericite 50 per cent. It was found that very little of the injected siliceous material was lost in the process of recovery from the skins. The skins of all rabbits were intact and presented no evidence that ulceration or abscess formation had resulted in any loss of the injected material. Very little evidence of transportation of the injected material from the original site of injection to the regional lymphatic glands could be found by gross examination and chemical analysis. As the loss of injected material cannot be accounted for by transportation, ulceration, abscess formation or by the recovery technique, it is assumed that the loss is due to solution and excretion in the body fluids.

It was found that at the end of one week almost as much loss of the injected material had taken place as at a period of six months. This early loss might be explained in two ways. The injected material, though ground to a very fine state of division, was not of uniform particle size. Many of the particles showed Brownian movement, and such particles may have passed into solution very rapidly. The other explanation might be the passage of these smaller particles into the circulating blood or lymphatic channels to go into solution in these fluids or to be excreted in particulate form.

(b) *Silicon.*—Silicon was used as a control since it had been found to be very inert when injected subcutaneously in animals. This was attributed to the fact that it was thought to be insoluble. In these experiments silicon gave a lower recovery than any of the other dusts used, with the exception of sericite. The fact that silicon should disappear to such a great extent could only be attributed to its solution or to the fact that it was the most finely particulate

of all the dusts and was "picked up" more quickly by the circulating fluids. There is also the problem of oxidation. The solubility of silicon might be appreciably increased by even the slight oxidation when it is dried at 110° C. Berzelius¹⁴ claims that silicon oxidizes readily when slightly heated in air and the extent of oxidation depends on the rate of formation of a protective crust of silica on the individual particles. A certain amount of oxidation of silicon also occurs in water, and therefore, probably, in the tissue fluids. Weiss and Engelhardt¹⁵ found that water at room temperature is decomposed by finely divided silicon ($\text{Si} + 2 \text{H}_2\text{O} \rightarrow \text{SiO}_2 + 2 \text{H}_2$).

It is also interesting to note that silicon is the only dust used the percentage recovery of which shows a definite relationship to the length of time in the animal. In six months, the recovery had decreased to 50 per cent. The sudden drop of 15 per cent which occurred within a few days might be explained by the excretion of the dust in particulate form, but 50 per cent over a long period can more reasonably be explained by solubility.

The solubility of this very finely ground silicon was determined by shaking 1 g. in 50 c.c. water in a bakelite tube in a water bath at 37.5° C. for 20 hours. The contents of the tube were then filtered and the silica in the filtrate determined colorimetrically¹⁶ and found to be present in a concentration of 50 parts per million—which is appreciable. When the other dusts were treated similarly silica was found in the filtrates in the following concentrations:

Albite	57	parts	per	million
Sericite	71	"	"	"
Microcline	73	"	"	"
Orthoclase	100	"	"	"
Talc	116	"	"	"
Oligoclase	120	"	"	"

It is interesting to note that the oxidation theory, mentioned above, involves the formation of silicon dioxide, and that if this occurs it is difficult to explain the lack of fibrosis produced by the silicon, particularly since silicon disappears from the site of injection more rapidly than quartz.

(c) *Sericite*.—It is also interesting to note that sericite is outstanding in having the lowest percentage recovery from the skins, the greatest change in the silica content after recovery, and also a slightly more marked tissue response than the other silicates. It is also appreciably soluble

in both water and Tyrode's solution. This is surprising, since other investigators have found sericite to be very insoluble and very inert.

The separation of sericite from underground sericitic schist has not been previously reported in the literature. Other workers have selected small pieces of pure sericite as it occurs naturally in underground and in surface rocks, but in this case it has been separated from sericitic schist where sericite is uniformly distributed in minute fibrous aggregates among other minerals. Therefore, the sericite separated from this rock may be quite different in character from that used by previous investigators. Sericite was prepared in this way from underground sericitic schist, since it was assumed to be the source of sericite in mine dust. Then again, sericite, being an intermediate product of mineral change from feldspar to kaolin, as a result of weathering, is not a mineral of constant composition, and might reasonably vary considerably. Also, there are two forms of sericite—fibrous and flaky. That used in these investigations was mostly fibrous.

Treatment with acid has been known to increase the solubility of silicates, *e.g.*, asbestos. This may be explained by the leaching of the silicate by the acid. Since sericite shows a greater change than the other silicates in its silica content after nitric acid treatment it is possible that the hydrochloric acid used in its preparation has changed its composition slightly from that used by other investigators. There is also the possibility that the fluids used for gravity fractionation might have been adsorbed to the surface of the finely particulate material and have had an effect on its solubility and a toxic effect on the tissue. This is unlikely, since the dust was well washed with volatile solvents and dried at 110° C., and since talc treated with the same fluids does not show the same low recovery from the skins or any marked tissue response.

Change in Composition.—

The small change observed in the per cent silica in the recovered material is quite comparable to that produced by the nitric acid treatment alone. The greater part of the change in the silica percentage is undoubtedly due to the acid treatment alone and not to the action of the tissue fluids.

The nature of the action of nitric acid resulting in an increased percentage of silica has not

been determined. If it be due to the leaching of Na_2O and K_2O (a point which we have not established, because the analysis for these elements is difficult and would be impracticable to do in such a large series), it must be only a partial leaching. The differences observed in the silica, aluminium and magnesium contents were much smaller than they would have been had much leaching of the basic constituents occurred.

The following table gives the quantity of alkali present in the various minerals. It is obvious that if much of the alkali had been removed by the tissues greater changes in the percentage of the other constituents would have occurred.

Theoretical K_2O and Na_2O contents of the following minerals:

	Percentage
Orthoclase	16.9 K_2O
Oligoclase	25.0 Na_2O
Microcline	16.9 K_2O
Albite	11.8 Na_2O
Sericite	11.8 K_2O

In this work it has been assumed that if the body fluids had a leaching effect on silicates a significant change would take place in six months. A change of 10 to 15 or even 20 per cent in the silica content as a result of the leaching of the basic constituents of the minerals was expected from some of the theories advanced, but, on the other hand, the lack of change agrees with the x-ray diffraction patterns of dusts which have been recovered from silicotic lungs.¹³ These patterns show no change from those of the original mineral dusts.

SUMMARY AND CONCLUSIONS

Seventy-five rabbits which had been injected subcutaneously with 1 gram samples of microcline, albite, sericite, orthoclase, oligoclase, talc, quartz and silicon of known composition and a high degree of purity were killed at the end of periods varying from one to six months. The dusts recovered from the skins by the digestion of the tissue in nitric acid were chemically analyzed again. One gram samples of the same dusts were treated with concentrated nitric acid

for the same length of time as the skins, then recovered and analyzed.

No marked change in the composition of the above silicates results from the action of the body fluids. The slight difference found between the composition of the recovered material and that of the original was probably caused by the nitric acid treatment.

The silicates used give evidence of solution in the body fluids. Listed in order of increasing solubility they are: albite, quartz, oligoclase, talc, microcline, orthoclase, silicon and sericite. Very little solution occurs after the first week.

In all cases the skins of animals injected with silicates or silicon show only a mild foreign-body reaction. Quartz produces a proliferative nodular response that becomes progressively more marked after two months.

The authors wish to express their appreciation to the Technical Silicosis Committee of the Ontario Mining Association for their financial assistance which has made this investigation possible.

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LIGHT THERAPY AND CARBOHYDRATE METABOLISM.—

L. Pincussen has found that ultra-violet and visible rays greatly influence the carbohydrate metabolism; the most obvious effect was a lowering of the blood sugar. He proved in animals that the decrease of the blood sugar goes side by side with an increase of the glycogen content of the liver and muscles and with a decrease of

the lactic acid, so that the ratio of carbohydrate to lactic acid increases and the glycogen which has disappeared from the blood is stored in the tissues. The rays therefore act in the same way as insulin. The effect of the irradiation depends, however, on its wave-length, and the amount of glycogen in the liver and muscles of irradiated animals.—*Arch. phys. Ther.*, Dec., 1937, p. 750. Abs. in *Brit. M. J.*

A HYPOGLYCAEMIC SUBSTANCE FROM THE ROOTS OF THE DEVIL'S CLUB (*FATSIA HORRIDA*)

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THIS paper presents data which show that from the roots of the Devil's Club (*Fatsia horrida*) an extract can be obtained that exhibits marked hypoglycaemic properties. The material is active when fed by the mouth and apparently has no marked toxic effects. Although the active material has not been isolated in the pure state certain observations lead the writers to believe that it is not identical with any insulin-like material of plant origin so far reported in the literature.

A large number of insulin-like materials, both synthetic and of plant origin, has been described in recent papers. For a review of these the work of Hill and Howitt¹ and of Braun and Rees² may be referred to. The most active of these substances appear to be derivatives of guanidine, and synthetic preparations such as synthalin (decamethylene diguanidine) have been made available commercially. A material of plant origin, but of unknown constitution, has also been marketed under the trade name "myrtillin". Three commercial preparations derived from guanidine and intended for the oral treatment of mild cases of diabetes have been favourably reported on by Frank, Nothmann and Wagner (synthalin),³ von Beznak and Hariss (anticoman),⁴ and by Hirsch (omalkan).⁵ The toxicity of guanidine derivatives appears to be the subject of some controversy,¹ but the data would suggest that up to the present no guanidine derivative has been prepared that does not show some toxic effects, particularly in regard to the liver and kidneys.

The extract investigated by the writers was prepared from the fresh or dried bark from the roots of the Devil's Club, a shrub that grows wild in great abundance along the coast of British Columbia. The extract is made by infusion with hot water. Such a preparation has long been used by Pacific Coast Indians, though for what specific purpose is not clear. Our attention was brought to this material through the examination by one of us of a

surgical patient, who, on hospitalization, developed marked symptoms of diabetes. This person, it was learned, had kept in apparent good health for several years by oral doses of an infusion of this root bark, and is in fact still leading a normal life with the aid of this infusion.

EXPERIMENTAL

Biological assays were carried out on white Belgian hares. In preliminary work a starvation period of twenty-four hours was allowed. Later this was extended to forty-eight hours, and in all experiments reported in this paper the animals have been starved for that period. Blood sugars were determined by the micro method of Folin.⁶ In control animals starved for forty-eight hours the blood sugar never varied more than ± 5 mg. per 100 c.c. from the initial starvation level for a period of six hours. The average variation was considerably less than this. However, only changes greater than 10 mg. have been taken as significant.

The work was done on a colony of 24 animals, 6 of which never received any extract and were used as controls in a pathological examination for toxicity. The remaining 18 were all used regularly for assay work, and, whilst considerable variation in individual response was noted, all the animals reacted in the same general way towards the extract. One circumstance, however, deserves to be mentioned here. During the earlier part of the work the animals were fed a diet which included a certain proportion of greens, together with oats and alfalfa. During the winter months the greens were left out of the diet, which for some 5 or 6 months consisted chiefly of oats and bran with water *ad lib.* After several months on this acid diet it was noticed that it was practically impossible to produce hypoglycaemia with extracts that had previously proved to be very active. Three days after the greens had been restored to the diet the extracts showed their original hypoglycaemic action. This observation corroborates that of Page.⁷

The following technique was finally adopted for preparing an extract suitable for investigation.

The bark was stripped from the roots either by hand or by means of an improvised ball mill, boiled three times with twice its volume of water, and the extract filtered off. Tannins were removed with neutral lead acetate and excess lead by means of hydrogen sulphide. The precipitated tannins, which came down in a gelatinous form, were separated by means of a Sharples super-centrifuge. The excess hydrogen sulphide was removed by boiling, and the extract finally evaporated, so that the number of c.c. of final volume was one-third the number of grams of the original bark. The extract was made slightly alkaline with magnesium oxide, filtered, and stored for use. Unless otherwise stated this extract was used throughout the investigation.

No systematic investigation has yet been made regarding the yield of potent extract that can be obtained from a given quantity of roots. Seasonal variations and the parts of the roots selected will undoubtedly be important factors. The following data may however give some idea of the yields we have obtained. The bark comprises from 10 to 20 per cent of the weight of the green roots, the larger roots giving the smaller yield. The moisture content of the bark averages about 70 per cent. In general we have found that an extract made from dried bark when made up to a volume in c.c. equal to the number of grams of the dried bark is of the same potency as one made from the green bark when made up to a volume in c.c. equal to one-third the number of grams of the original green bark. Over two hundred assays have been made with this extract. These data are too numerous to report in detail. Typical data have therefore been given in the form of charts.

Effect on alimentary hyperglycæmia.—Two starved rabbits of similar weight were fed 1.0

c.c. of 50 per cent glucose per pound of body weight and the rise in blood sugar was followed every half-hour. This was repeated once a week for five weeks. In every case a curve similar to those given in Chart 2 was obtained. The same rabbits were then fed the same amount of glucose and in addition an oral administration of a simple water extract of dried Devil's Club root bark in amount equivalent to 0.4 gram of the dried bark. Three repetitions of this experiment gave blood sugar curves similar to those shown in Chart 2.

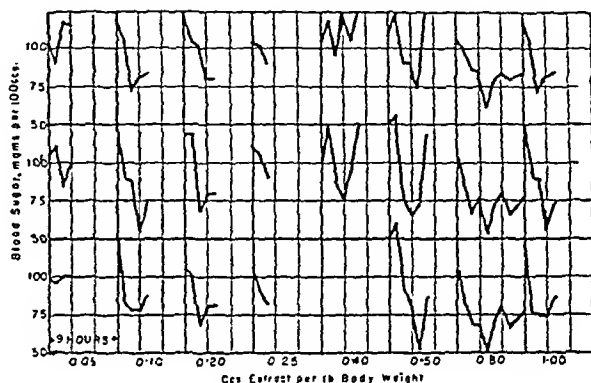


Chart 1.—The hypoglycæmic effect of graded doses.

With glucose alone a maximum rise of about 45 mg. glucose per 100 c.c. of blood was reached at the end of the first hour. At the end of the second hour the original blood sugar level had not been reached. When the extract was fed with the glucose the maximum rise was but 25 mg. and this was reached at the end of the first half-hour. Thereafter the blood sugar fell rapidly, and at the end of an hour and a half was more than 25 mg. below the initial starvation level. Usually the initial starvation

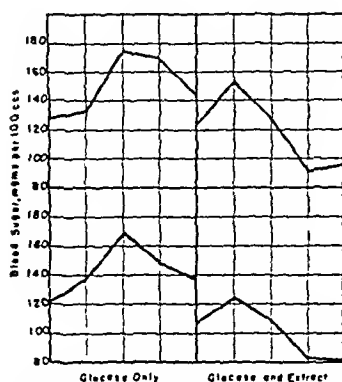


Chart 2.—Effect on alimentary hyperglycæmia.

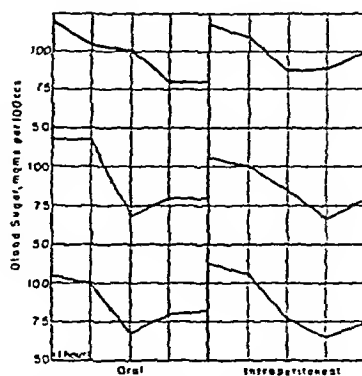


Chart 3.—Oral vs. intraperitoneal administration.

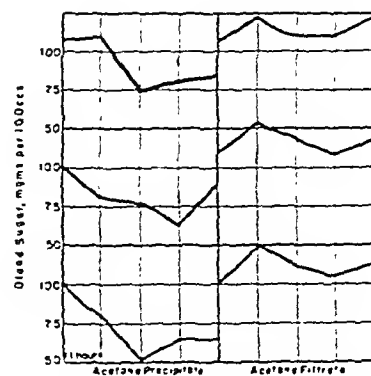


Chart 4.—Separation of hypoglycæmic from hyperglycæmic principle by acetone.

level was not reached again until after the third hour.

These data are conclusive in showing that the extract contains a substance very active in reducing alimentary hyperglycæmia.

The hypoglycæmic effect.—The tannin-free concentrated extract was then fed to starved rabbits without administration of glucose. The extract was given orally by means of a graduated pipette in amounts based on the body weight of the starved rabbit. Blood sugars were determined immediately before giving the extract and at hourly intervals afterwards. A few typical data are given in Chart 1. At a level of 0.05 c.c. per lb. of body weight the results were not conclusive. In some cases a noticeable drop in blood sugar occurred, but in others there was either no effect or a slight initial rise. At levels of 0.1, 0.2 and 0.25 c.c. per lb. of body weight a rapid hypoglycæmia was produced, with a reduction of the blood sugar of 35 to 70 mg. per 100 c.c. At levels of 0.4 and 0.5 c.c. per lb. of body weight some peculiar results were obtained. In nearly every case an initial rise in blood sugar was noted, followed in most cases by a very rapid drop. At these higher doses however there was nearly always a decided fluctuation in the blood sugar values which would lead one to suspect that in the extract a substance was present that had a hyperglycæmic effect which only became noticeable above a certain level. Even at these high doses we have not yet succeeded in producing coma, although rabbits with blood sugars below 60 mg. per 100 c.c. were always extremely lethargic. With doses of 0.8 and 1.0 c.c. per lb. of body weight the erratic behaviour of the blood sugar was more pronounced, but in general the gross hypoglycæmic effect was lengthened.

It might be mentioned here that although a standard starvation period of forty-eight hours was used, the oral feeding of the extract sometimes produced results that differed markedly in identical rabbits used at various times on the same dose. These variations, however, were not individual variations but occurred in groups. For instance a group of three rabbits might give an average lowering of the blood sugar of 50 mg. in three hours, taking five hours to return to the initial starvation level. A week later the same three rabbits, on the

same diet and starved for identical periods, when fed the same dose of exactly the same extract might give a lowering of 65 mg. within two hours but return to the original starvation level in three hours. The room in which the rabbits were kept varied in temperature within very wide limits, especially during the winter time, and we are inclined to think that this variation may have been an important factor in this peculiar behaviour.

The toxic effect of the extract.—Twelve rabbits were selected for a toxicity test. Six of these 12 had never been given the extract. They were fed the colony diet and were used as controls. Six other rabbits were fed 1 c.c. of the concentrated extract daily for five months. At the end of this time the twelve rabbits were killed and the livers, kidneys, and adrenals were sent to Dr. H. H. Pitts, pathologist at the Vancouver General Hospital. Dr. Pitts kindly examined these organs for us and has given us permission to quote the following from his report:

"We have made a great many sections of each block and have stained the liver sections for fat, and, while I believe there is no question that there is definitely more fatty degeneration in the livers of those animals who have had the extract, I do not consider that it is of any significant amount, for in some of the sections of the controls there is almost as much and in sections of different blocks from the same specimen of the experimental ones there is practically no degeneration, so that it is apparently a very patchy type and apparently not of any particular pathological significance."

Since the livers of some of the control animals showed as much fatty degeneration as those from the animals which received the extract the above report would appear to indicate that the extract was without any marked toxic effects. However, the extract used in these experiments was not pure and contained besides the active material some gums, sugars (0.6 per cent as glucose), magnesium acetate, a small amount of magnesium hydroxide and possibly other natural contaminants. Among these contaminants must be included a hyperglycæmic principle. A single isolated example which we have never been able to duplicate will illustrate the activity of this latter substance.

Three starved rabbits were given 1.0 c.c. per lb. of body weight of the standard tannin-free concentrated extract. Blood sugars were then determined hourly with the peculiar results shown in Table I.

TABLE I.
HYPERGLYCEMIA PRODUCED BY DEVIL'S CLUB ROOT EXTRACT

Rabbit No.	Wt., lb.	Starvation	Blood sugar, mg. per 100 c.c.							
			1st hour	2nd hour	3rd hour	4th hour	7th hour	8th hour	9th hour	24th hour
13	11	133	278	182	250	256	250	172	244	87
14	11.3	118	222	200	244	256	244	182	227	111
19	8	111	250	196	222	244	250	182	200	95

The same three rabbits have since responded normally to smaller doses of the extract. Other rabbits when fed this high dose have given results similar to those shown in Chart 1. So far no explanation has been found for these results, for even when the hyperglycæmic factor (see below) is separated from the hypoglycæmic factor the rise in blood sugar is not so pronounced as in the present case.

Oral vs. intraperitoneal administration.—Oral and intraperitoneal doses have been compared at levels of 0.2 c.c. of concentrated extract per lb. of body weight. Some comparative data are plotted in Chart 3. There is not a great deal of difference between the results of the two methods of administration. The average lowering is approximately 40 mg. from the starvation level for both methods. The rate of fall is also about the same for each method.

Separation of the hypoglycæmic from the hyperglycæmic factor.—In an effort to purify the concentrated extract attempts were made to precipitate the active constituents. It was found, eventually, that the hypoglycæmic substance was less soluble in dilute (30 to 40 per cent) acetone than in water. By diluting the extract with water and then adding acetone to bring the concentration up to about 40 per cent, an amorphous precipitate was thrown down, whilst the sugars, gums and organic salts were retained in solution. The precipitate and filtrate were freed from acetone by vacuum evaporation and made up with water to the original volume of the undiluted extract. These two extracts were then biologically assayed at a level of 0.2 c.c. per lb. of body weight. The results given in Chart 4 indicate that the precipitate undoubtedly contained the hypoglycæmic factor, depletions in the blood sugar of from 35 to 50 mg. being obtained. After four hours the blood sugars were still much below the original fasting level. In the case of the filtrate a hyperglycæmia of 20 to 25 mg. was produced within the first hour and, although this hyperglycæmia slowly disappeared during the next two hours, no hypoglycæmia

was ever produced. The sugar present in the extract is too small to account for this rise in blood sugar, and it has been assumed that the hyperglycæmic factor remains in the filtrate.

The precipitate thrown down by the dilute acetone is insoluble in neutral or slightly alkaline media, although in the original extract it appears to remain in solution. It is soluble, however, on slight acidification, a fact which suggests that the unknown material is basic in nature. Another fact which bears out the above observations is that on long standing the concentrated alkaline extract gradually deposited a small amount of an amorphous precipitate which on biological assay appeared to have a greater hypoglycæmic effect than the solution itself. The amount of precipitate so far obtained has been too small to do much with in the way of identification. It is planned to obtain larger amounts of it and to subject it to a systematic chemical examination. Clinical trials of the extract on diabetic patients under adequate control are also to be undertaken in the immediate future.

The writers wish to acknowledge their gratitude to their technician, Miss Norma Rogers, whose assistance has been invaluable in accomplishing the large amount of routine laboratory work. They are also deeply indebted to Dr. H. H. Pitts, of the Pathological Department of the Vancouver General Hospital, for his generous cooperation in preparing and examining sections for the toxicity tests. Finally, their thanks are extended to the Fisheries Research Board of Canada for the use of an unused room in the Fisheries Experimental Station in which a large proportion of the experimental work was carried out; and also to Mr. Kitagawa for supplying the first information regarding the raw material.

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PRESENT DAY PROBLEMS IN THE MANAGEMENT OF DIABETES*

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IN coming to London to speak about diabetes it gives me a feeling of intense satisfaction to recall that a fellow Canadian received in this city the inspiration which led to the most outstanding advance in the treatment of diabetes. In the nearly sixteen years since Banting gave us insulin its value has been appreciated more and more. Yet many patients still fail to receive the full benefit which they might derive from insulin treatment, and likewise fail to secure effective dietary treatment by modern methods. The purpose of this paper is not to present any discovery but to discuss simple rules in regard to diagnosis and treatment which may help in the everyday care of diabetic patients.

The seriousness of diabetes is fully realized when a patient who has previously been perfectly well fails in health rapidly and succumbs to coma. Fortunately, such an occurrence is becoming rare. It seldom occurs except when there has been obvious neglect on the part of the patient and his family, or blind dependence on unsound means of treatment. Today the harmful effects of diabetes more often develop in less conspicuous fashion. It is the patient who looks quite well, and feels fairly well, yet with diabetes only partially controlled, who may be destined for disaster. Such an outcome should be avoided if the aims of treatment are critically examined and the consequence of inadequate therapy considered.

THE AIMS OF TREATMENT

The objective of diabetic therapy is three-fold. First, the treatment should restore the patient to good health and keep him in good health. Second, the treatment should permit him to live a useful and contented life. Third, it should, if possible, abolish glycosuria and hyperglycemia. It is often difficult to fulfill all three aims completely. They overlap to some extent but sometimes seem to come in con-

flict. Drastic treatment imposed to secure normal reports from the laboratory can make a patient feel both miserable and discontented. The physical well-being of the patient should be placed first. It is almost as important to keep him in good spirits, since one cannot expect a patient to submit indefinitely to a regimen which he finds irksome and intolerable. Control of hyperglycemia and glycosuria throughout every part of the twenty-four hours is desired but has in the past not always been considered imperative.

Restoration of health can be brought about by any diabetic regimen unless long-standing disease has caused irreparable harm. The patient can be kept reasonably contented if a study of the individual requirements and tastes is made. Yet prevention of some degree of hyperglycemia and intermittent glycosuria often fails with the methods available up to the present time. Consequently, many patients and some physicians wonder why it is important to make the attempt. The physician who expects his patients to keep "sugar-free" must be prepared to answer this question, since it is constantly before him, even when it is not expressed. The possibility of maintaining more successful control of glycosuria by the new slowly acting insulin preparations makes it even more important to appreciate the advantages of adequate treatment.

THE RESULTS OF INADEQUATE TREATMENT

The risk of coma scarcely needs emphasis. The patient suffering from severe diabetes which is not well controlled must realize that acidosis and coma may quickly develop if an accident or complication should supervene. In addition, there are four other reasons why the control of the disease should be as complete as possible. If the urine contains sugar constantly vitality is often impaired. The patient may think he is well, and some patients even boast that they feel better when they have a little sugar in the urine, yet it is much more common to find lack of energy and lack of endurance. There is sometimes striking evidence of the

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effect of diabetes on the gonads. Menstrual changes and amenorrhœa appear in women and impotence is a not infrequent complaint in men. These effects on the sex organs may well be duplicated in other organs of the body, the change in function of which cannot so readily be recognized.

Failure to control glycosuria may result in retardation of growth of diabetic children. Many children seem to thrive surprisingly well even though they have high blood sugar, and hence glycosuria, a large part of the time. Yet I cannot feel that it is good policy to permit this deliberately. The effect on growth has brought about actual dwarfism in some cases, and it cannot be sound judgment to depend simply on good luck to prevent this misfortune.

Failure to control glycosuria permits progression of diabetes which might otherwise be avoided. It is a common observation that, in the early cases particularly, complete control of glycosuria and hyperglycæmia tends to bring about recovery in greater or less degree. On the other hand, persistence of glycosuria and hyperglycæmia tends to result eventually in progression to the severer grade of diabetes. The patient who hopes to get along without insulin injections must make sure that the glycosuria is controlled. Otherwise, the disease will tend to develop, sometimes slowly, but often rapidly, to the point at which control can be brought about only by daily treatment with insulin.

Failure to control diabetes leads to complications of various types. Patients with uncontrolled diabetes have increased susceptibility to infection and to degenerative changes in the arteries, nerves and retina. Uncontrolled diabetes may, in addition, intensify other diseases which may develop. For all these reasons intensive treatment should be undertaken to keep diabetes under control.

Success in the management of diabetes depends to a large extent on the way in which the situation is handled in the beginning. Adequate treatment applied immediately may spare the patient serious trouble later on in the course of the disease. It may permit control with much greater ease and simplicity. It may also have an important psychological influence. One often finds it difficult to deal with a patient whose diabetes has for a long time been half treated, even though he may need attention badly. It

is much easier to secure cooperation and maintain the interest of the patient if systematic treatment is employed right from the start. Emphasis should, therefore, be placed on institution of satisfactory treatment immediately after the diagnosis of diabetes has been established.

PROBLEMS IN DIAGNOSIS

The diagnosis of diabetes is usually made easily. The symptoms are characteristic and the laboratory tests are simple. Yet it is now well known that one can by no means depend on the symptoms to make the diagnosis of diabetes. In a large percentage of cases no symptoms are present at the time the disease is discovered. Consequently, it can be detected only by routine examination of the urine in cases in which absence of symptoms would arouse no suspicion. Glycosuria without diabetic symptoms was formerly often dismissed as of no importance. Now the careful physician will always investigate further, and the next step is determination of the blood sugar. If glycosuria is associated with a high blood-sugar level (0.14 per cent or higher fasting, or 0.17 after a meal) it indicates the presence of diabetes.

If blood sugar tests are not made to permit certain classifications of the glycosuria prolonged observation is the necessary alternative. A patient who has had unexplained glycosuria, even though only transitory, should not be dismissed from observation until diabetes can be excluded, since it is so important to recognize diabetes in the early stages. Frequently the blood sugar test is omitted because it may seem inconvenient or expensive. In the long run it will prove wise to make the blood test, so necessary in establishing early diagnosis.

If evidence of diabetes is found the patient must have diabetic management for the rest of his life, and it should be decided once and for all whether the patient has true diabetes mellitus or glycosuria of a harmless type. The problem may be compared to the situation with regard to syphilis. Everyone realizes the importance of making an accurate diagnosis of syphilis before instituting treatment. If the diagnosis of syphilis is made the patient must undertake treatment throughout several years of his life. If the diagnosis of diabetes is verified the patient and physician are committed to a course of treatment and supervision which

affects the patient's entire lifetime. Considering syphilis and diabetes only from the standpoint of health, the consequences of erroneous diagnosis are equally serious. One cannot afford to make a mistake in either case.

It is important to avoid beginning treatment until one is certain that the patient has diabetes. If glycosuria is found in a case in which there are no symptoms of diabetes no change in the diet should be permitted until the blood sugar test has been made. If the patient, on advice, or because of his own fear, avoids eating the usual amount of carbohydrate, the glycosuria may disappear and the blood sugar may become normal as well. The change of identification of early diabetes by the first blood sugar test is lost. One cannot assume that the patient is free from diabetes. The blood sugar test must be repeated after the patient has again returned to a full diet. It may even be necessary to perform a sugar tolerance test when otherwise it might not have been needed.

A sugar tolerance test is helpful if the routine sugar tests are normal, or if they are on the borderline. In applying the sugar tolerance test it must be remembered that the nature of the response may be influenced greatly by the nature of the diet which the patient had eaten previously. The patient should have a normal diet for at least one day before the test is performed.

It is a common mistake to advise trial of restriction of the diet when any sugar is found in the urine. When the patient returns later and glycosuria is absent, it may then erroneously be concluded that he has had a benign glycosuria or, if he has had true diabetes, that the condition has subsided so that there is no need for further attention to the matter. The subsequent history of cases in which this mistake has been made indicates how blind a decision of this sort may be. It is extremely important that treatment be not started until the diagnosis is definitely made.

INDIVIDUAL REQUIREMENTS IN TREATMENT

The treatment needed is dependent upon the requirements of the individual case. The general principle consists of the provision of a diet which will maintain good nutrition, and, in addition, the administration of insulin if glycosuria tends to persist when a suitable diet is employed. A large percentage of the older pa-

tients have diabetes of mild degree which can readily be controlled by simple dietary regulation. Yet the mere fact that a patient is beyond sixty years of age does not justify laxity in treatment. A considerable number of elderly patients have diabetes of such severe degree that insulin is needed in large dosage, and the maintenance of good health and safety depends on thorough attention to treatment. The patients in whom diabetes develops before the age of thirty are likely to have more severe diabetes, and in such cases insulin is almost always required when the disease has been present for more than a year. However, juvenile diabetes sometimes runs a benign course for the first year or even longer. Nevertheless, the potential danger can never be overlooked; there is a tendency toward progression even in the absence of complications, and if the situation is complicated by some unusual condition rapid change to a severe diabetic state may occur. For this reason every diabetic patient under the age of thirty years should be trained in regard to the use of insulin, even though it may not be needed at the start. In children, special care is essential because the disease may be so deceptive, and, apart from the danger of loss of life, the risk of poor development must be considered.

The exact nature of the diet is not a matter of profound importance. Every physician who deals with many cases of diabetes tends to develop his own scheme of diet planning. One may expect good results in following any one of these. The thing which is important is to make sure that the patient is able to use the diet with or without insulin so that the urine is kept free from sugar. The diet must also be planned in such a way that it will reasonably satisfy his appetite and desires as well. In order that patients may not get a wrong conception of the matter, I believe that the term "dietary restriction" should be abandoned and dietary regulation substituted in speaking of the dietetic therapy of diabetes.

READY-MADE DIABETIC DIETS

The ready-made diets illustrated in Table I have served to make the prescription of dietary regulation a simple matter. The A, B or C diets are used depending on the amount of carbohydrate desired. The number 2 menu in each series is suitable for the average person; it

TABLE I.
DIABETIC DIETS

	A			B			C		
	1	2	3	1	2	3	1	2	3
Carbohydrate	75	80	80	112	120	120	145	153	163
Protein	50	65	65	55	70	80	58	74	86
Fat	60	115	170	42	108	185	42	108	187
Calories	1,040	1,615	2,110	1,046	1,732	2,465	1,190	1,880	2,679
Food									
Egg	1	1	1	1	1	1	1	1	1
Meat	90	120	120	90	120	150	90	120	150
Bacon		15	15			15			15
Cream, 20 per cent....	90	240			240			240	
Cream, 40 per cent....			240			240			240
Butter	15	30	40	15	30	50	15	30	50
Vegetable, 5 per cent..	400	400	400	400	400	400	200	200	200
Vegetable, 10 per cent.				200	200	200	200	200	200
Orange or equivalent..	300	300	300	300	300	300	450	450	450
Cereal				15	15	15	15	15	30
Potato							120	120	120
Bread	30	30	30	60	60	60	60	60	60
Milk	240	240	240	240	240	240	240	240	240

DIRECTIONS

Use one of the "B" diets to start treatment, "B-1" for an obese patient, "B-2" for an average patient, "B-3" for a young, thin patient who needs more nourishment. Use insulin if necessary to control glycosuria and hyperglycemia.

If it is desired to use less carbohydrate to facilitate the control of glycosuria at the beginning, use one of the "A" diets.

If more carbohydrate can be tolerated or is desired, use one of the "C" diets.

In each case use the number 1 menu when a reduction diet is needed, the number 2 menu for the average patient, and the number 3 menu for patients who need more calories.

Adjust the diet to suit the needs and desires of the patient by making suitable additions and deductions.

Changes in calories can be made easily by altering the amount of butter in the diet. One square of butter, 10 gm., furnishes 75 calories.

can be easily adapted for patients requiring either less calories or more calories, by making the changes as shown in the example in Table II. Any of these diets may serve as the framework of an initial diet which can be later adjusted to suit the needs of the individual.

ADJUSTMENT OF INSULIN DOSAGE

Insulin is indicated whenever the diet selected fails by itself to check glycosuria. The action of insulin varies greatly in different individuals and the dosage must be determined by trial in each case. If the urine contains sugar in every specimen throughout each day the total dosage of insulin should be increased; if some specimens contain sugar while others are sugar-free there is probably need, not for a larger amount of insulin, but for redistribution of the doses. Once the urine has become free from sugar, blood-sugar tests are of great value in determining the best distribution of the dosage in relation to meals, and as a rule it is an advantage to have the blood-sugar test made during the day rather than in the morning before breakfast, as is the usual custom. A test made at 11 a.m. or at 4 p.m. will help to indicate the size of dose which should be employed before

the subsequent meal, and will give warning when the threshold of hypoglycemia is approached.

PROTAMINE ZINC INSULIN

The relatively short duration of the action of the individual dose has been considered one of the chief difficulties in the artificial supply of insulin by hypodermic injections. Hope of solving this difficulty came with the discovery by Hagedorn that the rate of action was retarded by combination of insulin with protamine and the additional effect of zinc, revealed through the work of Scott, of Toronto. The new preparations of insulin possess advantages of unquestioned value, yet they cannot replace ordinary insulin entirely. Their effects lack flexibility to meet the demands for more intensive insulin action which may come after meals. Even control of diabetes can best be secured when protamine zinc insulin is combined with rapidly acting insulin, supplied either by the pancreas of the patient or by supplementary injection of unmodified insulin.

Protamine zinc insulin thus yields best results in the treatment of diabetes of relatively

TABLE II.
DIABETIC DIET B-2

CARBOHYDRATE 120, PROTEIN 70, FAT 108—CALORIES 1,732

Breakfast

	Grams
Orange, medium size, $\frac{1}{2}$ cup.....	100
Cereal, a small serving.....	15
Egg, one	20
Bread (or toast), 1 small slice.....	10
Butter (1 square).....	120
Cream, 20 per cent, $\frac{1}{2}$ glass.....	

Mid-day meal

Meat, a small serving.....	60
Vegetables	
2 servings 5 per cent, each $\frac{1}{2}$ cup.....	200
1 serving 10 per cent, $\frac{1}{2}$ cup.....	100
Bread, 1 small, thin slice.....	20
Butter (1 square).....	10
Fruit, 1 serving (10 g. carbohydrate).....	60
Cream, 20 per cent, $\frac{1}{4}$ glass.....	120
Milk, $\frac{1}{2}$ glass.....	
Coffee or tea.....	

Evening meal

Soup, clear broth if desired.....	60
Meat, a small serving.....	
Vegetables	
2 servings 5 per cent, each $\frac{1}{2}$ cup.....	200
1 serving 10 per cent, $\frac{1}{2}$ cup.....	100
Bread, 1 small thin slice.....	20
Butter (1 square).....	10
Fruit, 1 serving (10 g. carbohydrate).....	60
Cream, 20 per cent, $\frac{1}{4}$ glass.....	120
Milk, $\frac{1}{2}$ glass.....	
Coffee or tea.....	

The B-1 diet (lower in calories for obese patients) is the same as the B-2 except for the omission of cream, meat 30 gm. and butter 15. Carbohydrate 112, protein 55, fat 42—calories 1,046.

The B-3 diet (higher in calories) includes in addition to the B-2 menu, meat 30 gm., bacon 15 and butter 20; 40 per cent cream instead of 20 per cent. Carbohydrate 120, protein 80, fat 185—calories 2,465.

mild or moderate degree. In cases in which 20 units of regular insulin would be used in two or three injections a single dose of the new preparation given before breakfast is effective. In more severe cases, requiring 30 units or more, substitution of the new insulin is not so simple. Here its slow action may fail to prevent postprandial hyperglycemia and glycosuria. Modification of the menu to give a more even distribution of the carbohydrate foods may help; less carbohydrate may be given at meal time, and part of the allowance given for afternoon tea and for an evening lunch.

In the most severe cases, protamine zinc insulin and unmodified insulin may both be needed. A patient requiring 60 units of insulin daily, for example, may require 40 units of the new insulin and 20 units of the old insulin before breakfast. Sometimes an additional dose of regular insulin must be given before

the evening meal, or perhaps before each meal. In the latter circumstances, the use of protamine zinc insulin may have no real advantage from the standpoint of convenience, although it may permit more complete control of the hyperglycemia.

The use of protamine zinc insulin may be disadvantageous at the time of sickness. Its slow action may fail to keep pace with sudden changes in the severity of diabetes. If the patient loses his appetite and fails to eat his full allowance of food there may be risk of hypoglycemia. A wise policy is to reduce the dose of protamine insulin one-half, and then supplement it by injections of regular insulin before meals, adjusting the dosage according to the results of tests of the urine. Five to 20 units may be used before each meal if sugar is present. If glycosuria persists on all tests the doses may be increased further, adding 5 units at each step; an extra 5 or 10 units may be given at bedtime also. The dosage may be increased boldly in the morning, but caution should always be used at the end of the day because of the cumulative action of insulin.

Hypoglycemic reactions from protamine zinc insulin are not likely to occur unless the dose is large, but there is always need for caution when the dose is more than 30 units. It is probably wise not to prescribe more than 40 units of protamine zinc insulin in one day, unless the behaviour of the patient is well known. When the dosage has been raised to this level an interval of one week should usually elapse before making further additions; supplementary injections of regular insulin may be used if necessary to check persisting glycosuria in the interval.

THE IMPORTANCE OF EDUCATION OF THE PATIENT AND MEDICAL SUPERVISION

Once the physician has determined the diet for the diabetic patient and, if it is needed, has prescribed insulin in the required dosage, successful outcome is dependent upon two additional factors. The patient must have sufficient knowledge to practise the regimen in his daily home life. The physician must maintain constant supervision so that in spite of changing conditions the control of diabetes may be adequate. Treatment should never be started until the diagnosis is certain, but, once begun, it should be continuous and complete.

ALLERGY IN CHILDHOOD*

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THE importance of allergy in the field of medicine, particularly in pædiatrics, can easily be appreciated when one finds that approximately from 7 to 10 per cent of our population suffer from some allergic condition.¹ Since a very large number of these manifest themselves in the first decade of life and respond more satisfactorily to treatment during this childhood period a general consideration of this subject should be of interest to all.

The history of this subject is interesting. With the use of diphtheria anti-toxin in 1894,² which sometimes resulted in serum sickness and occasionally death, the first investigations in the field of allergy were begun. Further observations in this field were made by Richet,³ Theobald Smith,⁴ Rosenau and Anderson.⁵ It was not until 1906,^{6,7} when von Pirquet coined the word "allergy" in relation to work done on serum disease in man and the tuberculin test, that this word became accepted as a definite medical term. His early definition was that, "Allergy indicated an altered reaction in the tissues of man to foreign proteins". Today, this term has come to mean, in its broad sense, "a hypersensitiveness to foreign protein". In other words, allergic people react in an abnormal way to something which is non-toxic to most of us.

Oriel,⁸ in his short and cleverly written monograph, states that "Diseases such as infantile eczema, hay-fever and asthma, now called allergic diseases, are really but symptoms depending upon an allergic state." He classifies these conditions due to hypersensitiveness to proteins, according to the place where the symptoms of the allergic reaction occurs, namely, the various systems of the body.

The theory of the mechanism of production of the allergic state is closely allied to that of anaphylaxis, and one should at this point become acquainted with such terms as antigens, atopens, antibodies and atopic reagins. Antigens are sub-

stances that can give rise to antibodies. Atopens and atopic reagins parallel this definition in the allergic sense. For discussion purposes one may say that the mechanism is primarily an antigen-antibody reaction (atopen-atopic reagin reaction), and that there are three possible states: (1) the normal, in which there are no antibodies; (2) immunity, in which the antibodies are free in the circulation; and (3) allergy, in which the antibodies are fixed in the tissue cells. The important factor in allergy is the strong hereditary predisposition to develop an increased permeability of the tissue cells.

Certain chemical reactions occur in the blood and tissues during an acute phase, and several that bear a relation to therapy may be mentioned here, such as a tendency to lowering of the blood sugar, a tendency to hypo- or a-chlorhydria; and a low blood calcium, which favours an increased permeability of the tissue cells.

DIAGNOSIS

The diagnosis of the allergic individual is made perhaps more from a careful and complete medical and allergic history than from the other supplemental aids to diagnosis at our disposal. These will be discussed later. The taking of the allergic history, as suggested by Bray,⁹ may be divided into predisposing factors, related to the onset of symptoms, and the precipitating factors, which are specific and non-specific, and are related to the production of an attack.

A. PREDISPOSING FACTOR (related to onset).—

1. Heredity—allergic predisposition has a strong tendency to occur in families.
2. Tissue trauma—severe illness before onset of symptoms, viz., asthma; (a) pneumonia; (b) infectious diseases—pertussis, rubella.

B. PRECIPITATING FACTORS (related to production).—

SPECIFIC

Absorbed by: (1) *inhalation*—animals, hairs, feathers, dusts, pollens, moulds and fungi; (2) *ingestion*—foods and drugs; (3) *injection*—sera, drugs, bites and stings; (4) *infection*—bacterial allergy and worms; (5) *contact*—fabrics, chemical and physical agents. These are carried by the blood to the shock organ, with resultant allergic reaction.

NON-SPECIFIC (Catalyzing Factors)

(1) *Dietary*; (2) *environmental*; (3) *toxic*; (4) *nasal*; (5) *psychic*; (6) *endocrine*; (7) *physical*; (8) *chemical*; (9) *mechanical*. These lower the "allergic threshold" so that specific substances may act.

* From the Department of Allergy, Children's Memorial Hospital, Montreal.

Read before the Pædiatric Section of the Medico-Chirurgical Society, March 12, 1937, Montreal.

Diagnosis is made by (1) careful medical and allergic history; (2) by various tests: (a) scratch cutaneous, (b) intradermal, (c) conjunctival, (d) nasal, (e) patch, (f) passive transfer; (3) elimination; (4) exposure; (5) diets.

Urticaria is the feature of a positive skin test.

The supplemental means at our disposal for completing our diagnosis are the various tests with the foreign proteins or atopens. These may be in powder, liquid form, or the substance itself. Hansel²⁰ defines several methods.

The *scratch cutaneous* tests consist of a series of scratches made on the arm or back, using N/20 NaOH (in children) or Coca's solution as a solvent. They are read in 15 minutes to 1½ an hour. A positive test consists of a wheal, surrounded by an area of redness accompanied by an itching sensation.

The *intradermal method*, using a tuberculin syringe, consists in injecting 0.02 c.c. of a dilution intraeutaneously 10 to 100 times weaker than that which just gives a positive scratch test.

The *ophthalmic* and *nasal* tests are obvious, and speak for themselves.

In the *patch* test the substance is placed in direct contact with the skin for 24 to 48 hours, and a positive test results in dermatitis. This test is particularly useful in contact dermatitis of the skin, when the individual is sensitive to various dyes, metals and drugs such as formalin, iodine, picric acid and novocaine.

The *Praustnitz-Kustner* reaction, or the *passive transfer* test, consists in "locally injecting the serum of the patient into a non-sensitive, normal individual, and then finding that the sites so prepared react with an immediate urticarial wheal when the corresponding protein is injected into them."

The most satisfactory test as to whether a condition is really allergic is the precipitation of an attack by bringing the person into contact with the particular substance to which he is thought to be sensitive. Elimination of probable offending atopens, in spite of negative tests, is frequently of benefit, as seen by the results of Rowe's elimination diets.

TREATMENT

The treatment of these cases in a general way should be as follows: (1) elimination of probable offending atopens; (2) avoidance of pets, animal danders, feathers, kapok and dusty atmospheres; (3) elimination of foci; (4) in food-sensitive patients, either eliminate, modify or substitute for the offending atopens; (5) if unavoidable, desensitization is used to neutralize the fixed antibodies—as pollens. In cases of hay-fever and asthma, etc., medications such as, adrenaline, ephedrine, potassium iodide, stramonium, and many other substances may have to be used as symptoms arise.

This study has been divided into cases manifesting symptoms in the various systems of the body. Most of the cases fall into groups of cutaneous, subcutaneous and respiratory allergies. The greater percentage of these condi-

TABLE I.
CUTANEOUS AND SUBCUTANEOUS ALLERGY

Diagnosis	Number of patients	Average age of onset (years)	Average age first visit (years)	Males	Positive family history	Positive percentage family history	Associated allergies								
							Asthma	Angio-neurotic edema	Dermographia	Eczema	Enuresis	G. I. Symptoms	Hay-fever	Papular urticaria	Urticaria
Urticaria.....	33	3.4	5.7	21	22	66	23	3	2	15	1	5	3	1	..
Eczema (Infantile).....	90	0.4	3.7	56	63	70	57	4	0	..	0	6	6	2	15
Papular urticaria.....	6	2.5	4.8	1	5	83.3	2	..	1	1
Angio-neurotic edema.....	7	4.3	5.2	5	5	71.4	4	4	1	..	3
Seborrhæic eczema.....	4	0.16	1.7	1	2	50	1

tions did not occur singly but were associated with other allergies. We found that a considerable number of patients developed their allergic manifestations, particularly asthma, following some severe infection causing tissue trauma. Of

eczema there were 57 cases associated with asthma and 15 cases with urticaria.

Gastro-intestinal allergy is a frequent complication of eczema and urticaria. It is interesting that the average age of onset for eczema is

TABLE II.
RESPIRATORY ALLERGY

Diagnosis	Number of patients	Average age of onset (years)	Average age first visit (years)	Males	Positive family history	Positive percentage family history	Associated allergies									
							Asthma	Angio-neurotic edema	Dermographia	Eczema	Eurestia	G. I. Symptoms	Hay-fever	Papular urticaria	Urticaria	Vasomotor rhinitis
Asthma.....	147	2.75	5.3	100	102	67.6	..	4	0	57	..	14	12	3	23	7
Hay-fever.....	18	6.7	8.6	16	14	77.7	12	1	..	6	..	1	3	..
Vasomotor rhinitis....	13	4.4	6.6	3	11	76.9	7	0	..	3	..	1	0	1	2	..

these, 8 had pertussis, 1 had rubella, 72 had sinus infection, 64 had diseased tonsils, 13 had pneumonia, 3 had diphtheria, and 1 child had asthma following the removal of a peanut from a bronchus.

0.4 years and that the sensitivity is predominantly due to foods.

RESPIRATORY ALLERGY

Note again how frequently asthma follows early infantile eczema. Hay-fever when it occurred was usually associated with asthma in this series of cases. The average age of onset in

CUTANEOUS AND SUBCUTANEOUS ALLERGY

It is noteworthy here that out of 90 cases of

TABLE III.
INCIDENCE OF FAMILY HISTORY

	Hives (33 cases)	Eczema (90 cases)	Asthma (147 cases)	Hay-fever (18 cases)	Vasomotor rhinitis (13 cases)	Seborrhæic eczema (4 cases)	Papular urticaria (6 cases)	Angio- neurotic edema (7 cases)
Maternal.....	4	18	25	2	2	..	3	2
Paternal.....	5	15	19	2	4	..	1	2
Bilateral.....	4	6	14	0	2
Maternal (distant).....	4	11	17	1
Paternal (distant).....	3	4	12	4
Bilateral (distant).....	0	0	3	0
Sister (only).....	0	3	4	3	1	1
Brother (only).....	1	4	6	1	1	1	1	1
Brother and sister (only).....	1	2	2	1
Total.....	22	63	102	14	10	2	5	5
Percentage positive....	66%	70%	69.4%	77.7%	76.9%	50%	83.3%	71.4%

PERCENTAGE OF MALES AFFECTED

Males.....	21	56	100	16	3	1	1	5
Percentage males.....	63.6%	62%	67.6%	88.8%	23.1%	25%	16.6%	71.4%

this group (mostly inhalant allergies) was much later than in the cutaneous group (mostly food allergies).

INCIDENCE OF FAMILY HISTORY
PERCENTAGE OF MALES AFFECTED

Our family incidence conforms with the findings of most authors, in that there is a very strong hereditary tendency to allergic diseases. Seborrhœic eczema, papular urticaria and vasomotor rhinitis occurred more frequently in females.

AVERAGE AGE OF PATIENTS AT ONSET

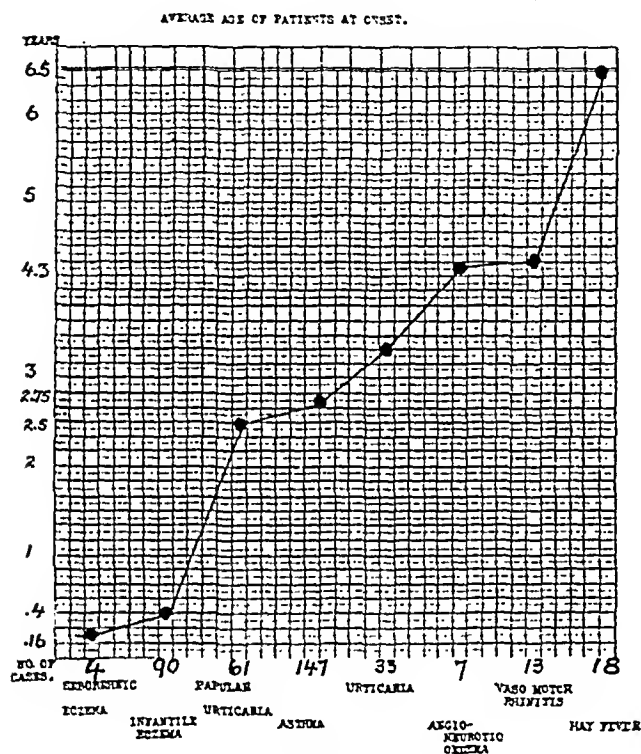


Chart 1

Our findings confirm those found by other authors, that the cutaneous manifestations occur early in life and are followed later on by the respiratory ones.

CUTANEOUS AND SUBCUTANEOUS ALLERGY
CAUSES, RESULTS

As a whole these manifestations did not respond readily or as satisfactorily to our treatments as the respiratory allergies. We feel that the dermatologist should be consulted as to the local care of these patients. In our clinic close cooperation between the allergy clinic and the dermatological clinic make for a better understanding and better treatment of the patient. If the cutaneous allergies are properly treated early the later allergies may be avoided to some extent and sometimes prevented.

GENERAL CONSIDERATIONS OF CUTANEOUS AND
SUBCUTANEOUS MANIFESTATIONS

Hives.—Skin tests are of some value in this condition. Elimination diets are perhaps more useful. Hives frequently occur, during or following some infection which lowers the allergic threshold, and only then does the patient react to the atopens to which he is sensitive. Hives occurred occasionally with asthma or hay-fever due to sensitivity to pollens.

Eczema.—This condition is one of the first warnings that we have that the patient is allergic. Since 57 cases of eczema were associated at some time or other, mostly in the later years, with asthma as a more serious complication, more serious attention should be directed

TABLE IV.

CUTANEOUS AND SUBCUTANEOUS ALLERGY

Diagnosis	Number of patients	Average age of onset (years)	Average age first visit (years)	Males	Positive family history	Positive percentage family history	Causes						Results						
							Food	Food and inhalant	Inhalant	Pollen	Bacterial	Unknown	Cured	75 per cent improved	60 per cent improved	25 per cent improved	Same	Not known	Not treated
Urticaria	33	3.4	5.7	21	22	66	12	8	0	8	15	6	2	1	1	4	4
Eczema	90	0.4	3.7	56	63	70	18	31	13	32	24	25	11	1	..	18	14
Papular urticaria	6	2.5	4.8	1	5	83.3	1	3	2	2	1	1	2
Angio-neurotic œdema . .	7	4.3	5.2	5	5	71.4	3	2	1	1	0	0	6	0	1
Seborrhœic eczema	4	0.16	1.7	1	2	50	1	1

to the eczematous child, particularly the causative agents, prophylactic and curative measures. Allergic mothers, or mothers of allergic children who wish to nurse their offspring, should follow an elimination diet, particularly of eggs, during pregnancy and the lactation period. Eosinophilia is a feature in most of these patients, one having as high as a 22 per cent count. Hives and eczema are frequently associated at their onset. These patients when admitted to the general wards, we found, were more subject

RESPIRATORY ALLERGY, CAUSES, RESULTS

We find here that the bacterial factors are of considerable importance in this group. It is felt that much can be done for this type of case, with proper investigation, treatment and co-operation on the part of the patient.

GENERAL CONSIDERATIONS OF THE RESPIRATORY ALLERGIES

Asthma.—This condition seems to occur earlier than any of the others in this group. It

TABLE V.
RESPIRATORY ALLERGY

Diagnosis	Number of patients	Average age of onset (years)	Average age at first visit (years)	Males	Positive family history	Positive percentage family history	Causes											Results						
							Food	Food and inhalant	Inhalant	Bacterial	Pollen			Unknown	P. Sinuses		Cured	76 per cent improved	60 per cent improved	26 per cent improved	Same	Not known	Not treated	
											Grasses	Weeds	Grasses and weeds		Single	Double								
Asthma.....	147	2.75	5.3	100	102	67.6	17	37	21	30	9	19	8	6	22	50	32	36	20	9	9	10	31	
Hay-fever.....	18	6.7	8.6	16	14	77.7	5	8	5	..	3	9	3	4	1	2	8
Vasomotor rhinitis	13	4.4	6.6	3	11	76.9	0	2	1	7	3	3	6	3	7	3

to respiratory infections and pneumonia. The eczema tends to disappear with the development of high fever, operations, and frequently disappears with the appearance of asthma, or vice versa. Intradermal and passive transfer tests are of definite value when scratch tests are negative. Constipation and teething are important non-specific factors, at which time the patient will not respond to treatment satisfactorily.

Papular urticaria.—We doubt whether this condition is a true allergic one. It is felt that bacterial invasion plays quite a rôle as an influencing factor in this manifestation. Three of the patients responded to vaccine therapy, and one disappeared following tonsillectomy.

Angio-neurotic œdema.—One of our cases, not included in this series, developed this condition on eating eggs. One developed angio-neurotic œdema of the eyes from the pollen of weeds, another from sensitivity to tobacco. The latter swelling was relieved with the injection of adrenaline.

Seborrhæic eczema.—From our experience we find it doubtful whether this condition is allergic; however, it is occasionally associated with some other allergic manifestation.

may be so mild that it is barely perceptible or so severe that a child may wheeze continually for years, causing marked deformity of the chest, and ultimately leading to bronchiectasis. Many of the patients lost their asthma after being hospitalized for a short time. Two children developed asthma during an acute otitis media. It quickly disappeared following a paracentesis. The question of vagotonia arises here. Teething apparently caused asthma in another child. High fever, high altitudes, operations and anæsthesia stopped attacks in some. Irritating odours, such as paint, turpentine, tobacco, and dusty atmospheres can precipitate attacks without the patient being sensitive to these atopens. Several of the patients developed asthma from food odours, particularly fish. Sensitivity to glue was not an uncommon offender. Symptoms occurred more frequently when the child went to sleep at night than during the day. Results with inducto-therapy seem to be encouraging in cases with parenchymal changes of the lungs, as seen in some of our cases.

Hay-fever.—This condition is a late manifestation of the respiratory allergies. The grass

eases responded more readily to treatment than the weed cases. Pollen treatment for the uncomplicated hay-fever sufferer is on the whole very satisfactory.

Vasomotor rhinitis.—We did not find this a common manifestation in our series of cases. Most of our cases were associated with a bacterial allergy, and responded well to vaccine therapy.

Allergic cough.—A cough coming on in allergic children, or children of allergic parents, occurs usually in early fall to late spring. These cases responded well to vaccine.

Bacterial allergy.—This occurs as a result of bacterial invasion. In some of the children suffering from asthma a cold, accompanied occasionally by fever, frequently preceded the attack. The delayed type of reaction to the intradermal tests was the characteristic here. The best results obtained with vaccine therapy were in those cases who gave a good local reaction with each injection of the vaccine. It is felt that stock vaccines, prepared by our bacteriologist, were as beneficial as autogenous vaccines.

Every child was carefully tested by the scratch method. Other methods were used when deemed advisable. However, the lack of space

has prevented the inclusion of these in this report.

CONCLUSIONS

Allergy in childhood occurs frequently. A general consideration and a review of our first 200 cases has been presented. A child with eczema should not be dismissed with the prescription of an ointment; the child with bronchitis, with a cough mixture; or the child with hay-fever, as suffering from a summer cold, and given nose drops. All should be carefully investigated and proper treatment instituted.

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MODERN TRENDS IN CHILD PSYCHIATRY*

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THIS subject, which your Secretary presented to me, is a very suggestive one. It is, however, one that presents considerable difficulties, because child psychiatry is such an inclusive and ill-defined branch of medicine. Faced with the difficulty of defining psychiatry, I should like to avoid the problem by suggesting that it be considered as that integral part of the art of medicine which has to do with the physician's knowledge of human nature, that knowledge which the family doctor intuitively uses in assessing the importance of signs and symptoms in his patients. He knows, for instance, that the complaint of pain does not always have the same significance, and that one patient will make light of the discomfort of a lesion that would

seriously alarm another person. He knows that in many cases the symptoms about which his patients complain are related not to any local lesion but to anxiety and frustration. With the advances in the sciences ancillary to medicine there has been a danger that the handmaidens would usurp the rightful place of their mistress. There has been a tendency for medical practice to become a matter of pooling the results of studies of heart, blood, lungs, gastro-intestinal tract, etc., while the patient as a human being has been forgotten. I suggest that the realm of psychiatry be taken as that humanity that makes people men and not just automatons, and not even merely animals.

It would certainly be foolish to undervalue the importance of the detailed study of special anatomical systems or diseases. What I am

* An address delivered before the Cornwall Medical Society, November 12, 1937.

urging is just that the forest be not lost sight of in the contemplation of the trees. It may occur to you that it would be enough to say that psychiatry is a study of diseases of the mind. That will do, provided it is allowed that mental functions are functions of the whole human organization and not merely of the nervous system. Practically mind and body cannot be separated. You cannot add the results of psychology, roentgenology, electro-cardiology, hæmatology, immunology, anatomy, biochemistry, and any number of other studies and get John Smith. The whole thing is something more than the sum of the parts. A simple illustration is offered by the consideration of water. One could study hydrogen and oxygen separately all his days and never understand water. The qualities of water are something beyond the qualities of hydrogen and oxygen. So the characteristics of a man are beyond the characteristics of his organs, and my suggestion is, that you consider psychiatry as the study of the failures of that organization or integration of life forces which gives man his humanity. This brings us to the position of saying that what the physician needs to be a psychiatrist is not so much a lot of extra knowledge as a different point of view. Briefly, it is the point of view of the old fashioned family physician as contrasted with that of the more extreme specialist.

One basic science that has been rather neglected in medical education is psychology. There is not time to discuss this subject, but I should like to say a little about it. Psychology has frequently been put in a ridiculous position by over-zealous advocates of particular schools of thought, and I fancy that many sensible men have felt that the whole subject was too fantastic for reasonable discussion. The behaviouristic and psycho-analytical systems of psychology have both achieved a great deal of notoriety, and the contentiousness of their protagonists has been such that sober consideration of their theories has been difficult. Probably they both contain much truth and much error; certainly both are over-systematized. People always seem to prefer error to indefiniteness, and the psychoanalysts have characteristically been possessed by an itch to explain everything under the sun, leaving no tag-ends of uncertainty. However, for working purposes the physician needs a tentative theory of psychology. I shall try to sketch the outlines of such a theory, but, for lack of time, it

will have to be such a rough sketch that it may not be very helpful.

From birth the baby shows certain tendencies, to seek nutrition and eliminate waste products, to be comfortable in security, and fearful in insecure positions. The energy that informs these tendencies can be called "instinct". It may be recalled that the manifestations of instinctive energy that the baby shows are shown by the amœba at the other end of the animal scale. The amœba also has the tendency to reproduce, and the potentiality for the development of this tendency must be present in some way in the human infant, too, but to discuss that question would lead us into a disputed field.

As the child grows he begins to show an increasing need for self-assertion. The instinctive needs for love and security and for self-assertion are the manifestations of the life-force which are of the most importance in the formation of his personality. To satisfy those needs he learns to conform to the pattern of behaviour that his parents set. I should like to emphasize, however, that the infant best learns to conform to his parents' wishes if that conformity brings him love and security. To force obedience by fear is to employ a two-edged sword. I cannot enlarge on this important topic, but I hope I can make that one theme real for you. It is to satisfy their instinctive needs that children learn first to conform to the style of their parents, and later to compete in activities suitable to their ages. To put it another way, they can learn but they really can't be taught. The mind of a child is not a blank slate on which lessons are to be written, but a selecting organizing agency whose aim is to fit together all the pieces of the jigsaw puzzle that life presents to it, and whose energy is provided by the child's needs for love, security, and self-assertion.

Realizing the inadequacy of this sketch, I must pass on to some of the problems that are met in psychiatric work with children. I shall attempt to give a rough classification based on etiology. For various reasons this is not a satisfactory way to classify such problems. For one thing, the cause is never simple. There is inevitably a combination of factors in the background of a psychiatric problem. Without some classification, on the other hand, material becomes too cumbersome.

Many difficulties arise as a result of emotional deprivation. I said before that children adopted

their parents' ways in order to be secure in the love of the parents. If parents are too poorly developed to expend love, if they really do not want their children, or if children are brought up without parents or satisfactory substitutes, it is as if the children were deprived of a sort of emotional vitamin. They are apt to remain immature, to fail to develop stable, robust characters. Never being identified with a family group, it is hard for them to fit into larger social groups; being cheated out of the love they need, they may try to gain attention in unwholesome ways. Many of the adults who are unreliable and unstable, whose employment records are unsatisfactory, who are continually disappointing those who try to help them, and who are often malingerers, liars and swindlers, in short, the psychopathic personalities, have a history of a loveless childhood. They have never learned to respect the authority of a father they loved, and, consequently, always tend to resent authority. They have never known the security of a home where they felt they really belonged, and, consequently, have never learned true self-reliance. And when an individual resents the authority upon which he is dependent he is always the rebellious child, whatever his age. Maybe A. E. Housman had something like this in mind when he wrote:

The day my father got me
His mind was not on me;
He did not plague his fancy
To muse if I should be
The son you see.

My father and my mother
Out of the light they lie;
The warrant would not find them,
And here 'tis only I
Shall hang so high.

A topic that is often discussed these days is whether children should be allowed to do what they like or not. It is a query that is out of order to my way of thinking. Discipline that is too strict and not tempered by love certainly produces bad results, but if children are brought up in the security of a good home they will want to do what their parents want them to do, by and large. Opportunities must be provided for the satisfaction of their instinctive needs. Too much repression, which does not give a child any outlet for his exploratory urges or his instinct for self-assertion, often means that the dammed-up energy shows itself in some neurotic or rebellious way.

"Disciplined self-confidence" is probably a fairly good term for what most parents want in

their children. The discipline can be achieved by consistent sensible training, if parents can gain their children's love and set them good examples. Self-confidence will grow if a child's activities are graded so that he meets with a fair measure of success. A couple of factors that actively undermine the self-confidence of children are worthy of notice in a psychiatric discussion—fear does this and ideas of shame or wickedness. These feelings can act as repressing factors and interfere with a child's opportunities for normal self-expression. Always when this occurs there is a likelihood of undesirable compensations.

Another etiological group, which, however, overlaps those mentioned above, is composed of problems due to errors and inconsistencies in training and to unwholesome suggestions. In a gross way, what I mean by inconsistent training may be illustrated by that common situation in which one parent is very lenient and the other very strict, or in which the behaviour that is encouraged as being "cute" when visitors are fussing over a child is punished as "cheekiness" when the family is alone and the parents tired. Under such circumstances it is obvious that it is hard for a child to learn what is acceptable behaviour.

The subject of suggestion cannot be treated with justice in a few words. Fortunately, in speaking to physicians, it is not necessary to enlarge on it. You all know how over-anxious parents can suggest food-fussiness and nervousness to a child, and how the importance of physical illness can be exaggerated.

There is another subject which I wish to speak about a little more fully. This is what can be called the matter of individual differences. As an illustration of one aspect of personality in which individuals differ widely consider intelligence. Psychometric examinations enable us to measure intelligence fairly accurately, and thus to determine how much individuals differ in intelligence. Now it is common to find that when the intellectual ability of a child is over-estimated so that he is expected to do school work that is too hard for him there is likely to be trouble. The child cannot understand the nature of his difficulty—he is probably just aware of a sort of undifferentiated misery. This feeling is, however, very frequently expressed as an illness. It may be chorea; I have known it to be asthma and tenesmus. In-

telligence is only one aspect of personality. Individuals also differ in the traits that are called temperamental, and differences in temperament may lead to misunderstanding and difficulty. For instance, the impatience of a vivacious, choleric mother may cause her to be continually criticising and scolding her more methodical phlegmatic son, with the result that he feels like a duffer and comes to believe that his mother has no use for him. Having come to such a conclusion, it is easy for the boy to turn to illness as a means of gaining his mother's sympathy and attention. The terms "introvert" and "extravert" have been in fairly common use recently. Their definition is rather difficult, but in a general way it is easy to recognize the difference between the extravert who is interested predominantly in the things and events about him, and the introvert, whose own feelings and imagination occupy a good deal of his attention. Often the adjustment of children is made difficult because of the failure of their elders to adjust the environment to suit their degree of introversion or extraversion. There are many aspects of personality in which individual differences are seen, and the subject is worthy of more time than we can devote to it tonight. I should just like to say in passing, that as more knowledge of endocrinology is gained the study of temperament will be greatly facilitated.

Another group of problems in this etiological classification is that in which conflicts of culture cause stresses to act on a child. The children of foreign parents frequently come to despise the old country ways of their homes without truly acquiring the ways of this country. This situation leaves them empty of ballast, so to speak, and in many cases of juvenile delinquency and neuroticism this factor is present. Further, there is likely to be a good deal of mental conflict in such cases. Children want to love their parents, and yet, in order to ingratiate themselves with their Canadian playmates, they are more or less forced to look down on all the customs that the parents represent. Similar mechanisms operate when the clash of cultures is between religious groups or social classes, or when country boys move into the city.

The effects of physical illnesses are very important in the formation of personality trends. Many mothers tell us that. One will say that Johnny was quite a model child until he had

diphtheria or until he injured his head, but that subsequently she could do nothing with him. A physician has always to be on the alert for a brain injury or encephalitis, but study of a group of these cases will show clearly that it is more often the mother's changed attitude than organic damage that is responsible for the altered personality. The sick child is given much attention during his illness and convalescence, and he escapes easily from the challenges that school and play offer him. After his illness his mother may be looking for residual effects and tell her friends in his hearing that she thinks he has changed. She may be afraid of checking him at all for fear of bringing on a relapse. If a child has been finding it at all difficult to keep up the pace set by his companions he is very likely to make use of the easy way out offered by the supposition that his illness has had bad after-effects.

This classification is, of course, very rough; there is over-lapping and incompleteness, but there is no time for further refinement. I should like to mention briefly another classification, that of complaints. I have as I went along indicated very briefly some of the mechanisms by which unwholesome situations can be translated into symptoms. Personality difficulties may be expressed by almost any symptom, but probably those most commonly met are pain, disorders of the autonomic nervous system (anorexia, food-fussiness, vomiting, and, less commonly, constipation or diarrhoea) or tremors (St. Vitus' dance is not uncommonly hysterical). The complaint may be simply nervousness, and then it is usually obvious what a big part maternal suggestion plays. More puzzling symptoms are those which may be described as regressive; it is as though the child were trying to remain a baby. Baby talk, bed-wetting and timidity may be found in such a case. Usually the most obvious explanation is that the mother subconsciously longs to keep her child from growing up. In other cases, because probably of differences in temperament, unwholesome repression or babying will result in aggressive behaviour, which is more likely to come to the attention of the police than that of the physician. The last group of symptoms I shall mention may be called compensatory. I think this term is fairly self-explanatory: the crippled child is likely to find undesirable ways of mak-

ing up his handicap unless his activities are wisely planned. The same situation pertains in the case of a child who is unusually small or who has any other characteristic that makes him off from the group.

I must apologize for the indefiniteness of this paper, but the extensiveness of the field to be

covered makes this almost inevitable. In closing, I should like to repeat that the important thing in psychiatric work with children is not so much the possession of special knowledge as it is alertness to the very important part that what we may roughly call "personality factors" play in the development of symptoms.

SOME OBSERVATIONS ON PETROUS TIP SUPPURATION*

(REPORT OF THREE CASES)

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THE index of any comprehensive work on the surgery of the ear now contains a subject which was not to be found prior to seven years ago. That subject is "petrositis". The literature is full of divergent views on the subject, largely due, because, as Almour¹ has suggested, "the various workers have seen and treated one or at the most a few types of petrositis." Agreement can only be reached when enough evidence exists on which to formulate sound opinion. This requires the careful report of every case bearing on the subject, particularly cases coming to autopsy, careful criticism of such case reports, and the embodiment of the conclusions in the latest presentation of the subject.

This paper presents in considerable detail reports of three different types of infection of the petrous bone. The first presents a condition of which I have not found a report in the literature. The other two are germane to the observations which follow the case reports.

Patient 1 died from meningitis due to an abscess in the neck which ruptured upward through the tip of the petrous bone. This case is unique in demonstrating that a huge abscess can be present in the neck below the inferior surface of the petrous bone without accompanying indications in the pharynx. Patient 2 presented the symptom-complex of petrositis outlined by Kopetzky and Almour.² Pain in and behind the eye and symptoms of acute meningeal irritation recurred several times. Several operations were performed with the purpose of improving the drainage, but no radi-

cal procedures were adopted to reach the apex either from within or without the petrous bone. The procedures adopted were always timed and governed by ordinary clinical judgment. The external rectus paresis persisted over twelve months and discharge from the ear over eighteen months. The patient made a complete recovery. The case is an illustration of the fact that recovery, even if very slow, is inevitable if the natural process is guided and not hindered by the surgical procedure. The patient was far away from home and relatives, was in the public ward, and received constant daily supervision by the surgeon in charge, aided whenever required by any extra consultant he desired.

Case 3 is a tragedy. There was a most extensive empyema of the tip of the petrous bone. In spite of the decision that this was occurring the patient did not present the typical picture until the terminal phase had set in. The autopsy showed an involvement of the petrous tip so great that recovery must have been impossible unless adequate drainage had been effected, and it showed that the empyema could have been reached by the route and method advocated by Kopetzky and Almour. However, an attempt to follow this technique might also have been followed by a sudden terminal meningitis. Whether or not this drainage would have sufficed to control such an extensive involvement is problematical. The literature contains reports of such cases where heroic measures have been successful; it is probably silent regarding cases such as this where radical measures have terminated unhappily.

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Read at the Sixty-eighth Annual Meeting of the Canadian Medical Association, Section of Oto-Laryngology, Ottawa, June 24, 1937.

CASE 1

(No. 38885).—A girl, 12 years old, died of meningitis two weeks after admission for severe cervical adenitis. Autopsy disclosed that a large abscess in the

neck had ruptured through the inner third of the petrous bone.

The history showed twelve admissions to hospital age ten months of age for cervical adenitis on the left side. As an infant of ten months she was in hospital for six weeks suffering from nasopharyngitis, lateral otitis media, and bronchitis. The Wassermann and tuberculin tests were negative. The second admission shortly afterwards was for acute cervical lenitis. The third admission was at thirteen months of age. There was a hard immovable lump the size of a walnut on the left side of the neck below the left ear. Operation revealed a broken-down cervical gland containing a large quantity of yellow pus. Fourteen weeks later a left mastoid operation was done. The entire mastoid was found broken down and filled with pus. A large sequestrum lying in this slough was lifted out, disclosing that a radical mastoid excavation had been created by the disease. In the depth was a cond sequestrum. It was not removed and the cavity was left wide open. The pathological report (No. 15, 1925), showed the mass removed to be 12 by 12 by 7 mm., and to consist of dead bone and granulation tissue. A guinea pig inoculated with some of this material developed extensive tuberculosis. The patient was discharged eight months later with the post-aural scar healed and the middle ear discharging slightly.

During the next ten years the patient was admitted nine times for surgical treatment of cervical lenitis. The final admission was on October 30, 1936, one week prior to admission acute otitis media was noted, with discharge from the opposite (right) ear and a recurrence of the left cervical adenitis. The former had subsided but the latter had violently increased. The patient was quite ill. Her cheeks were flushed and her face had a pained expression. There was a faint suggestion of weakness of the left side of the face; otherwise the cranial nerves were intact; there was slight neck rigidity, a bilaterally positive Kernig, and the Brudzinski sign was positive. The post-aural scar on the left side was quiet. The area below the left ear and behind the jaw was hard, swollen and acutely tender. The pharynx was quiet. On account of the previous history tuberculous meningitis was considered the probable diagnosis. The meningeal signs increased. Nine days after admission the cerebrospinal fluid had a pressure of 191 mm. of water, and a cell count of 910, of which 12 per cent were polymorphonuclears; culture after forty-eight hours yielded hæmolytic streptococci.

Eleven days after admission there was hyperæsthesia over most of the skin surface, including the arms and legs; double vision at times; movements of the eyes were poor because of pain; bilateral ptosis; two days later marked right divergent strabismus developed, with weakness of both abductors, most marked on the left side; still, slight left lower facial palsy. Cerebrospinal fluid—pressure 250; blood-tinged; cell count 110; polymorphonuclears 38 per cent. Culture showed hæmolytic streptococci.

All signs and symptoms increased and the patient died on the sixteenth day. Autopsy showed acute hæmolytic streptococcal meningitis and a chronic cervical abscess (hæmolytic streptococci in pure culture) with a track to the base of the skull. Beneath and behind the left ear was a small, thin, healed scar over the mastoid area; it was neither reddened nor swollen. Over the whole of the base of the brain was a light coloured jelly firm layer of purulent material.

On the superior surface of the left petrous bone, and overlying the hiatus Fallopii, there was a small, rough, red area on the external surface of the dura about three-quarters of a cm. in diameter. As the dura was further reflected, thick, creamy pus welled upward into the left middle fossa through an erosion (0.5 cm. in diameter) in the left petrous bone about 0.5 cm. posterior to the foramen ovale. This defect was situated in the path of the groove for the greater superficial petrosal nerve and was 1 cm. medial to the radius transmitting this nerve. Pressure on the left

side of the neck caused an increase in the flow of pus through this aperture. An abscess cavity was opened in the neck which had the shape of an inverted pyramid with its base lying on the bare bone on the inferior surface of the petrous portion of the left temporal bone and its apex extending down into the neck. There was at least 1.5 cm. of firm tissue between the posterior pharyngeal surface and the nearest part of the abscess pocket. Just posterior to the left external auditory meatus there was a small depressed area of smooth, bare bone about 0.75 cm. in diameter on the lateral surface of the temporal bone. No communication could be established between this area and the abscess cavity.

CASE 2

(No. 64180).—A boy, 12 years old, was admitted January 17, 1932, after a simple mastoid operation, because of persisting pain in and profuse discharge from the ear operated upon and external rectus paresis on the same side.

An acute middle ear which was opened October 22nd was followed fifteen days later by typical mastoiditis. A simple mastoid operation was performed on November 6th. Two weeks after he was sent home with the canal and wound still discharging. Five days later pain in the ear and slight fever developed. The afternoon temperature ranged from 100 to 101° F. Ten days after discharge he was re-admitted and the mastoid cavity was re-opened and eurented on November 30th. In spite of this the discharge and intermittent pain in front of the ear continued. The post-aural wound was kept open and was almost dry, but there was considerable discharge from the meatus which at times was thick, purulent and greenish. Eighteen days after the second operation he complained of pain in the back of the neck, *in the left eye and behind it*, and there was a paresis of the homolateral external rectus. One month after this he was transferred to Toronto to the Hospital for Sick Children.

January 17, 1932.—The boy was in fair condition but extremely nervous and irritable; complete left external rectus paresis. The mastoid excavation was wide open, nearly healed and quiet. A small quantity of purulent discharge occasionally could be wiped from the front of the antrum. The left meatus was filled with thick, yellow purulent discharge which re-appeared in quantity from lumpy sensitive granulations. X-ray was considered by the radiologist not to show involvement of the petrous bone, but in spite of this a clinical diagnosis of an extradural abscess near the tip of the left petrous was made. Dr. Barraclough diagnosed onset of meningitis.

January 23rd.—Third operation; mastoid cavity explored under anæsthetic. No track was found. On January 26th power and tone were good; the optic discs normal; more movement in left external rectus. Then a sudden rise of temperature to 103.6°.

January 27th.—Fourth operation. Radical mastoid operation was completed; middle fossa greatly exposed. Other than the Eustachian tube no track for the pus was found.

On February 4th at noon the patient felt something flowing in the wound. The dressing was found more than usually soaked with pus. The wound was full of pus, the source apparently being the Eustachian tube. The left external rectus paresis almost gone. Following this the temperature was almost normal for over two weeks.

February 22nd.—Temperature 104°. Great pain in neck and back. No field defect; some paresis of left external rectus. Symptoms of meningitis. Wound not draining adequately. These symptoms persisted for four days. February 28th, much improved. The temperature was down and there were no signs of meningitis. Wound draining well again. March 30th, discharged from hospital. Slight discharge from middle ear. General condition very good. Still slight external rectus paresis.

June, 1934.—Middle ear found healed; for how long, unknown.

The boy is without signs or symptoms and very well.

CASE 3

(No. 5719).—A girl of 17 years had been subject for years to attacks of sore throat accompanied by purulent discharge from the left ear. She was first seen on the evening of January 3, 1936, toxic and acutely ill.

A head cold about December 22nd was followed by a nasty sore throat and discharge from the left ear. The surgeon in attendance had seen her frequently and had examined her carefully on the morning of January 2nd. The patient had had a chill on January 1st and a temperature of 103°, but the temperature was now normal. He dried out the ear thoroughly and observed it for about ten minutes, then gave his opinion that her indisposition was due chiefly to the throat infection and that a mastoid operation would be avoided.

On January 2nd there was another chill. On January 3rd there were two chills; the temperature had risen to 104°. The patient was very toxic and the nurse and the mother thought she had become rapidly and alarmingly worse. Her pharynx was moderately inflamed; the left antrum was dullish; the left ear was full of thick pus, and after being dried out the pus re-appeared in quantity; the retinal veins were distended; there were no external signs of mastoiditis. A diagnosis of acute mastoiditis was made, and a simple mastoid operation performed. The cortex was extremely hard, very thick, and acellular. The eell partitions were dense, but the mastoid cells and the antrum were filled with soft grey granulations or thick pus. The zygomatic region was much more cellular and involved similarly to the mastoid relatively far forward. A specimen from the mastoid was described as chronic osteomyelitis, but no growth was reported from culture. Blood culture was negative.

Following operation the patient's general condition rapidly improved. The discharge from the mastoid was so irritating that the stitches were removed on the third day and the wound thereafter kept wide open. An abscess over the left zygoma developed and was drained on the 8th day, and the temperature steadily dropped to normal. Thirteen days after operation, although the wound was still open and discharging, the patient was considered fit for discharge. During that night, however, she experienced a sharp pain in her head which she could not localize, and the next morning did not feel well, so her discharge was cancelled, and that afternoon (January 18th) her temperature rose precipitously to 105° and she became drowsy. There was considerable pain in the left side of the face, some pain behind the left ear, and a slight swelling over the left zygoma. White blood cells 11,000.

The patient was seen by an otologist and by a neurologist. Petrositis was considered on account of the persistence and quantity of the creamy purulent discharge from both middle ear and mastoid antrum, but there were no other signs or symptoms. The temperature fell rapidly; the drowsiness disappeared, but the patient developed a left frontal headache with discharge from the left middle meatus; there was neuralgic pain in the left upper teeth and the left maxillary sinus failed to illuminate. Ragged purulent masses were washed from the left maxillary sinus.

On the 22nd she looked improved and read a book. White blood cells 6,000. The zygomatic area was quiet and healed. Creamy pus continued to appear in the depth of the canal and the anterior part of the left antrum. For a week the temperature remained about 99° F. but she was not doing well; at times chilly; pain fluctuating between face and neck; appetite poor; coughing occasionally. The left maxillary sinus was washed every other day for a total of six washings, but as the discharge remained profuse and milky it was given permanent drainage through the naso-antral wall, after which it rapidly became clean. The patient still looked well but she complained of a vague feeling of stiffness or soreness of the neck on movement, and she

noticed that her vision was blurred and the right side of the tongue felt funny.

At midnight on February 5th the stiffness of her neck was quite severe for about 2½ hours, requiring 1½ grains of eodeia for relief. The temperature was normal. Very little discharge was seen in the mastoid antrum, but thick purulent discharge was still coming from the depth of the canal. There was no nystagmus and no choking of the optic discs. The next morning the temperature was normal, but the patient was definitely flat, did not want her breakfast, but ate some and then vomited. White blood cells 9,300. Dr. G. F. Boyer and Dr. K. G. McKenzie saw her in consultation. No new signs or symptoms were elicited, but it was decided that an intra-cranial complication was threatened, probably from petrositis, and that relief by drainage should be attempted. Dr. McKenzie considered that involvement of the posterior fossa was probable.

At operation the excavation was converted into a radical cavity, and the middle ear found full of granulations. The tympanic cavity was thoroughly cleaned. The root of the zygoma was healthy and very solid; it



Fig. 1

was heavily reduced so as to thoroughly expose the orifice of the Eustachian tube. Almost the entire inner table of the mastoid process was removed, exposing the lateral sinus and the dura of the posterior fossa. The tegmen was extensively removed and the dura of the middle fossa was gently raised. A fistula at the mouth of the Eustachian tube was searched for but not found. A probe passed along the superior surface of the petrous bone failed to reach soft bone or to indicate pus. Operation had failed to reach the focus responsible for the patient's symptoms.

On the day following operation the patient was drowsy but improved. The pain in the neck had gone and she moved her head quite freely. She refused everything but water. On the next day she noticed a slight pain above the left eye, was drowsy most of the day, was nauseated at times and vomited greenish fluid.

Following the radical operation the temperature reached normal on the 18th. At first she had considerable pain behind the eyes and reading made her nauseated, but these discomforts were diminishing. Then began a change for the worse. The headache became more severe, at times intense, and pain was

complained of behind the right eye. The stomach became more rebellious. Nausea became frequent. She refused nourishment most of the time, and yet she was bright occasionally. Light hurt her eyes. White blood cells 11,200; hgb. 63 per cent. In the evenings severe headaches occurred and there was increasing nausea and some vomiting.

On February 22nd temperature was 104.2°; less photophobia; more drowsiness; slight paresis of the left external rectus; a slow drift of the eyes to the right when the patient looked to the left; more vomiting. Right abdominal reflex gone. Visual fields uncertain, probably not impaired; commencing choking of discs. Suggestion of slightly less coordination with the left hand and arm than with the right. White blood cells 22,000. It was decided that a crisis was at hand and that probably a cerebellar abscess was developing. Cerebrospinal fluid smear showed a few pus cells and very many Gram-positive cocci in pairs and chains. Culture grew *S. hæmolyticus*.

The patient's condition rapidly became worse and she lapsed into unconsciousness. Dr. McKenzie injected air into the ventricles, and then explored for

and Bacteriology, to both of whom I am indebted for their painstaking efforts. They concluded that the terminal meningitis did arise from a break through of the tip of the left petrous bone into the middle fossa. The Gasserian ganglion was extensively infiltrated. The cavernous sinus was not involved.

"The serial sections do suggest that the involvement of the petrous tip can be traced back through the petrous bone to the middle ear. We would describe the track from the middle ear internally as being through the cells around the Eustachian tube, around the carotid canal, in front of the superior semicircular canal; not behind the semicircular canal. From general study of serial sections of this petrous bone we are of the opinion that there is present a chronic suppurative osteomyelitis with abscess formation, as is evidenced by the chronic reaction about some of the collections of pus, and also some new bone formation. Apart from these areas there are others in which there are collections of pus cells, with destruction of bone, and no evidence of fibrosis. It would seem, therefore, that there were present two types of reactions—a chronic suppurative reaction with a more recent acute suppurative flare-up supervening."



Fig. 2



Fig. 3

cerebellar abscess which was not found. The patient failed to rally following operation and died at four a.m. on February 23rd on the sixty-third day of her illness, and fifty-one days after the original simple mastoid operation.

Autopsy was performed four hours after death. There was a large amount of pus in the subarachnoid space over the base of the brain. There were no localized areas of softening in the brain.

Fig. 1 shows the floor of the skull with the openings made by the operations. At the tip of the petrous portion of the temporal bone, in the middle fossa, there was a small sequestrum of bone. This was irregular in outline and measured approximately 1 by 0.3 cm. The petrous portion of the temporal immediately about this area was apparently involved in an acute osteomyelitis.

Immediately after the brain had been removed an x-ray photograph (see Fig. 2) was taken, and then a probe was passed through the external meatus toward the region of the Eustachian tube mouth, and readily went into the tip of the petrous. The second x-ray (see Fig. 3) was not accurately centred but does show the probe in position.

The mastoid, petrous bone and meninges on culture grew *S. hæmolyticus*.

An extensive study of the petrous bone was undertaken by Dr. Gregor McGregor, under the supervision of Prof. W. L. Robinson of the Department of Pathology

DISCUSSION

Suppuration in the petrous bone both is and is not a new pathological and surgical entity. In 1893 Bircher³ is said to have successfully drained an abscess in the petrous apex by following a fistulous tract from the middle ear. In 1904 Gradenigo⁴ made observations which caused clinicians for the next twenty years to be constantly on the outlook for patients showing symptoms supposedly due to involvement of the petrous tip. In 1919 Sir Charles Ballance⁵ in his masterly work, "The Surgery of the Temporal Bone" shows a sketch illustrating an empyema of the tip of the petrous bone secondary to otitis media in a patient of 14. Unfortunately no date is given. He also refers to statements by Habermann⁶ and Körner⁷ that acute suppuration of the tympanum may give rise to osteomyelitis of the spongy portions of

the petrous bone, and he defines the latter as the bone immediately surrounding the labyrinth and in the vicinity of the bony portion of the Eustachian tube. He gives four illustrations of "the extension of purulent infection to the petrous" but in each case the picture and text suggest that the lesions were dependent upon labyrinthitis and did not involve the area internal to the internal auditory meatus. But, in spite of this, careful search of many other English and American textbooks of otology printed prior to 1926 shows that "petrositis"—or anything suggesting "suppuration of the petrous tip"—is not to be found in the indexes.

The picture suddenly changed. On June 30, 1929, Eagleton,⁸ performed the first operation of deliberately entering the petrous apex upon a patient whose condition had been diagnosed previously as "suppuration within the petrous apex". This was shortly followed by the first authoritative text on "The Suppuration of the Petrous Pyramid" by Kopetzky and Almour.

The present literature has established a clinical picture of a disease which has probably always existed, and has propounded various surgical measures for its relief. The past few years have seen much serious study of the normal petrous bone which have resulted in modifications of the classical descriptions of the bone, so that a statement of the present conception of its morphology must now be given.

THE NORMAL PETROUS BONE

The petrous bone is the horizontal inward projection of the temporal bone containing the inner ear and the horizontal part of the internal carotid artery. Its very name carries significance. It is of stony hardness. Within this stone-like bone lies the inner ear, further protected by its own shell of still more stone-like bone. The latter acts as a barrier to invasion by disease from the middle ear. Cavities within the petrous bone have long been known. Variation in their number, size and distribution were effectively demonstrated by corrosion preparations by Bezold⁵ in 1882 and Siebenmann⁶ in 1897, but disagreement regarding whether the cavities were marrow spaces or air spaces, and where the latter originated has existed until recent months. Certainty regarding the histological structure of the petrous bone has now been achieved for the first time.

Anson,¹¹ at the instigation of J. Gordon Wilson, has only last year exhibited at Toronto

the first model of air cells in the petrous bone reconstructed from serial sections by the method of Born. In this he has demonstrated air cells arising from the tympanic cavity near the point of continuity of the latter with the Eustachian tube and which passing inward almost surround the carotid canal and penetrate toward the tip of the petrous bone. The main area of the tip is made up of marrow cells. The air cells of the apex are interconnected continuously and they do not connect with the marrow spaces. Wilson¹² finds no extension of mastoid air cells medial to the internal auditory meatus. Guild,¹³ from histological section only, has postulated the picture of the petrous bone now presented.

"The outstanding feature of the pars petrosa of the temporal bone is its extremely wide range of 'normal' variation. This variation concerns not only size and external configuration but also the nature and arrangement of the internal structure. Some petrous pyramids have extensive complete pneumatization—the cells may be large, small or medium-sized; other petrous pyramids have no pneumatization. . . .; and every possible intermediate degree of pneumatization occurs.

"The structure of non-pneumatized portions of partially pneumatized pyramids is also variable. . . . The petrous pyramid is frequently made up of a mixture of pneumatized spaces, solid bone, cancellous bone with red marrow and with fatty marrow; there is no regularity to the arrangement of these tissues with reference to each other.

"The framework of the petrous pyramid, exclusive of the otic capsule, usually consists of so-called cancellous (or spongy) bone with a cortical layer of varying thickness. This cancellous bone has irregular trabeculae and septa which form the boundaries of irregularly-shaped spaces. These spaces are filled with one or the other of four things: hematopoietic (red) marrow, fatty marrow, a mixture of red and fatty marrow, or air-containing cavities. Histologically the marrows in these spaces are indistinguishable from the corresponding types of marrow in other bones of the body. The walls of the air-containing cavities are indistinguishable histologically from those of the mastoid region. The cavities have a very thin mucosal lining (or mucoperiosteum) that consists of a scantily vascularized layer covered by a simple squamous epithelium. Also, in both the mastoid process and the petrous pyramid, when there is only a partial pneumatization, this thin mucosa sometimes rests directly upon marrow-containing spaces.

"The regions of the temporal bone first pneumatized are the Eustachian tube, the middle ear and the mastoid antrum. Pneumatization of the mastoid process takes place by extensions from the mastoid antrum."

Guild now goes on to say:

"While pneumatization of the mastoid region is always by an extension of cells from but one of the primary areas, pneumatization of the . . . petrous pyramid may and does occur by the extension of cells from all three of the primary areas."

J. Gordon Wilson takes issue with him here and is having reconstruction models made to trace the origin of the air cells of the petrous. The first of these, by Anson, demonstrates an air-track to the Eustachian orifice. So far,

therefore, only one of Guild's three primary areas has been proved.

THE BEARING OF THIS MORPHOLOGY UPON THE SURGICAL PROBLEM

If Guild is correct the problem of surgical drainage of the petrous tip is complicated and uncertain. If Wilson is correct suppuration of the petrous bone is a complication of otitis media and not a complication of mastoid infection; then the correct surgical approach will be to expose the Eustachian opening and the floor of the middle ear as adequately as possible.

Surgically, it is correct to curette and break down infected pneumatic areas, but it is wrong to curette infected osteomyelitic areas. It has been shown above that the petrous bone is a mixture of pneumatic and marrow-containing elements. In so far as the latter are pathological it is wrong to attempt to curette them, while if the former are infected it may be right to do so, but right only if a surgical approach can be safely made.

This problem must be viewed from yet another angle—that of the method by which the petrous tip may be infected. It is reasonable to suppose that the air cells are infected *via* their point of origin in the mouth of the Eustachian tube. The marrow cells may become infected from infected adjacent air-containing cells, or their infection may be a true osteomyelitis of independent origin. In either case, when an empyema of part of the petrous tip exists, the problem arises of whether the surgeon shall make his approach, (1) outside the petrous bone; (2) through the petrous bone, or (3) restrict his interference to the exposure of the Eustachian tube area.

The literature contains descriptions of surgical techniques permitting an infected petrous apex to be opened from without *via* either the middle or the posterior fossa. Approach *via* the middle fossa can be made safely only to within a few millimetres of the Gasserian ganglion: from then on there is almost certainty of rupturing the arachnoid, with inevitable meningitis. When fortune favours, the surgeon may encounter an extradural abscess, in which event he will be able safely to drop probe or curette into the petrous tip and the subsequent recovery will be due to the fact that the pathological process had walled itself off. Approach *via* the posterior cranial fossa is even more hazardous. Lempert¹⁴ has described a technique which

allows the exenteration of the entire petrous apex under direct vision without injury to facial nerve, internal ear, dura, or carotid artery, but his ingenious but time-consuming operation has not yet had adequate trial. The intra-petrosal approaches are those of Ramadier¹⁵ and Almour (*loc. cit.*). The former involves the exposure of the ascending limb of the carotid artery, and the petrous apex is then approached beneath the knee of the carotid artery. The latter is by many considered difficult and dangerous.

THE TRUE INCIDENCE OF PETROSITIS AND THE PRESENT EPIDEMIC OF PETROSITIS

Fatal meningitis following an acute infection of the ear has been so relatively rare that the ear surgeon has looked upon it as a tragedy. It is, therefore, a fair statement to make that when an autopsy has been performed there has always been the keenest search to find the route of the infection. The condition of the dura mater overlying the petrous bone and that of the exposed faces of the petrous bone have been subjected to the closest scrutiny. It is very unlikely that gross break through of the petrous tip has been overlooked in the pathological department of any great hospital. In the last fifteen years, in a series of 3,425 consecutive autopsies at the Hospital for Sick Children, Toronto, which includes a goodly number of intracranial complications of otitic origin, suppuration of the petrous tip has been discovered in one case only.

The Ear, Nose and Throat Department of the Royal Infirmary, Edinburgh, in three papers by Hewat,¹⁶ Boyd¹⁷ and Fraser¹⁸ has published the results obtained in 1,279 consecutive cases of mastoiditis which came to operation, including minute details regarding all those which had intracranial complications and reports of all those which came to post-mortem during a period of over twenty-five years. It is significant to note that only one case of meningitis following apicitis was discovered. In attempting to obtain a true viewpoint regarding the subject of this paper it is impossible to overlook this long series of consecutive cases and its implications. Three speculations may be made regarding the rarity of petrositis in the Edinburgh series. (1) Petrositis may have been present in some of the cases which came to autopsy but was not discovered: (2) petrositis may have occurred in some of the fatal cases on which no post-mortem was obtained: (3) petrositis may have been

present in some of the cases of intraeranian complication which recovered.

The first speculation may be dismissed as untenable. The thoroughness of the pathological investigation at the Edinburgh Infirmary has left nothing to be desired, and their Ear, Nose and Throat Department led the English-speaking medical world in the histological investigation of the temporal bone. The second speculation must remain a possibility. But only 7 of the fatal cases were without post-mortem. Even were we to postulate that all these were cases of petrositis it would make the incidence of petrositis in a large clinic only 8 out of 1,279 cases in over twenty-five years—an incidence far below what is indicated by the present literature.

Thirdly, as has already been pointed out, petrositis has only been recognized clinically in the past few years. Sporadic cases had been described but they had been so rare that the symptomatology remained unknown. But there has been nothing to indicate that the true incidence of acute otitis media and of its complications has altered. Therefore, it is probable that among the recovered cases a number of cases of petrositis did occur—a number proportionate to the cases of mastoiditis in that twenty-five year period. And, if we admit that, we must conclude that the disease petrositis is one from which recovery will take place nearly always if a thorough mastoid operation is properly done, and properly handled after operation without any specific unlocking of the petrous pyramid.

The argument will be made that from the time of Gradenigo's description of his syndrome in 1904 claims were made that the syndrome of otitis media, pain, usually with a temporo-parietal distribution, and diplopia due to the involvement of the abducens nerve was indicative of extension of infection in the tip of the petrous. Granted. But even these cases were rare, as evidenced by the admirable paper of H. G. Esteourt.²¹ However the years have shown that the Gradenigo syndrome is not synonymous with infection in the tip of the petrous. There is probably no otologist of experience who cannot testify to sixth nerve paralysis being frequently transient. Transient sixth nerve palsy is a sign to which the neurological surgeon pays but scant attention for localization of a lesion.

The diagnosis of petrositis rests in part upon the roentgen-ray picture. The latter may be taken in the antero-posterior, vertico-mental or oblique diameters, but the depth of the petrous bone in the skull and variations in its structure make the picture difficult to read. In spite of this, whenever an otitis media or a mastoiditis is attended by signs which warrant x-ray study a special plate should be made to show the condition of the petrous. It should be realized, however, that in actual practice it is not possible to have x-rays taken in more than a small percentage of cases of acute mastoiditis. The suggestion of E. P. Fowler, Jr.,²² that a record of the exact technical factors used (*i.e.*, milliamperage, kilo voltage, tube distance, exposure time, etc.) should be kept, so that subsequent films can be reproduced with the same technique, is valuable but Utopian.

The literature abounds in x-ray pictures showing changes in the petrous bone, and the x-ray evidence seems to have been the factor which decided operation in some of the recorded cases. However, Coates *et al.* (*loc. cit.*) have shown by x-ray that suppuration in the petrous pyramid is not rare in patients requiring the simple mastoid operation and that spontaneous recovery is the rule. Therefore, while the x-ray has been a malevolent influence in abetting radical surgery it is now having a beneficent influence in proving that the conservatism of the past has not been too faulty. Let me suggest that x-ray study of the petrous should be confined to cases where the clinical picture suggests the possibility of suppuration in the petrous. Such x-ray will be of greatest value if it is definitely negative, for then the patient may be spared an unnecessary and possibly calamitous operation.

It is my belief that Kopetzky and Almour have made a real contribution to otology in presenting a picture by which involvement of the petrous apex can be recognized clinically, but it is my conviction that the long record of otology demonstrates that the majority of suppurations in the petrous pyramid tend to drain and heal spontaneously.

NOTE.—An extensive bibliography has been prepared, and is being included in the author's reprints. The small numbers in the text refer to this.

TWO CASES OF BILATERAL SPONTANEOUS PNEUMOTHORAX*

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FROM a review of the literature it would seem that cases of bilateral spontaneous pneumothorax are of sufficient rarity to warrant the presentation of two new additional cases. Kjaergaard¹ found only three cases of this condition in apparently healthy people; we here present another of these. Markson and Johnson² report a very interesting case; Hamilton and Rothstein³ report one of alternating bilateral pneumothorax complicating the collapse treatment of an active tuberculosis patient. A similar case has been reported by Sprague,⁴ while a report of a fatal case complicating pneumoconiosis is given by Schlomovitz and Glickman.⁵ Additional cases have been reported by Wilson,⁶ with a fatal outcome, and a chronic case affecting the apices, by Bryce,⁷ who also gives details of an exceedingly interesting case of delivery of a living child in a patient on whom a bilateral pneumothorax had been established in the course of treatment for pulmonary tuberculosis. To these we wish to add the following two cases.

CASE 1

P.H., Canadian, white, female, aged 16, a school-girl.

Previous history.—Measles, mumps, whooping-cough, chicken-pox and scarlet fever as a child, mild influenza in 1930. She otherwise had always been healthy. She was not susceptible to colds. In 1932 she fractured her left humerus while skiing. In November, 1933, while attending school, she felt suddenly faint during the recess hour, became short of breath, and vomited. When seen later in the day she was in bed and suffering no discomfort, but complaining of weakness on attempting to get out of bed. Physical examination disclosed a collapsed left lung which was confirmed three weeks later by x-ray. No lesion was apparent in the film to account for the condition, nor did she at any time have cough or fever. She remained in bed for two months and the lung fully expanded. Following this she was in good health until November, 1935, when she was seen by Dr. W. H. B. Munn, with a collapse of the opposite side (right). She made an uneventful recovery from this, and early in 1936 was sent to the Muskoka Hospital, where no evidence of tuberculosis or other disease could be found to account for the condition. These findings were substantiated by the Ontario Government Chest Clinic in September. She is now, apparently, in the best of health.

CASE 2

A.H., housewife, a Finlander, white, aged 53. Her previous history was difficult to obtain owing to the

lack of an interpreter, but her first husband and two sons died of tuberculosis and her present husband has an active lesion. Four other children have not as yet reported to the clinic for investigation. She presented herself to me at the out-patient department complaining of weakness and inability to do all her housework. Physical examination disclosed a large, well nourished woman, not in great distress, but with a marked malar flush; temperature of 100°; pulse 140. Her chest appeared emphysematous. It was hyperresonant on both sides and the movements were limited. The breath



sounds were distant but remarkably clear. The left chest was full of crackling râles scattered throughout. She was admitted for observation, and an x-ray taken (Fig. 2), which showed a bilateral partial pneumothorax affecting both lungs in their entirety. There was the typical picture of tuberculous infiltration of both sides of the lung, more marked in the left side. Under treatment her temperature fell slowly to normal, with occasional exacerbations to 99°. Her chest showed increasing movement and the breath sounds became clearer. On September 15th x-ray showed both lungs expanding well, there still being a moderately small pneumothorax at the costo-phrenic angle on the right side and a smaller one on the left (Fig. 1). Nine days later the patient was sent to the Haileybury Hospital, feeling quite well and with normal pulse and temperature. In connection with this last case it is interesting to note

* From the Clinic of Dr. H. M. Young, Anson General Hospital, Iroquois Falls, Ont.

that McMahon⁸ gives the cause of this condition in 58 per cent of cases to be tuberculosis and the outcome usually fatal. When last seen this patient seemed to be well on the way to recovery.

These two cases represent two separate types of this unusual condition. The first allows no conclusion to be drawn as to its cause, and one is forced to accept the "valve-vesicle" theory of Kjaergaard. The second case is undoubtedly due to tuberculosis, and most of the reported cases fall into this classification.

Wilson and Sinclair give the following classification. "The etiology of bilateral spontaneous pneumothorax is not definitely agreed upon. Among the causes may be mentioned: (a) rupture of tubercles on the surface of the lung; (b) rupture of emphysematous bullæ; (c) an inherent fragility of the surface of the lung; (d) fistulization through the mediastinum between both pleural cavities; (e) a possible

anatomical deformity in the development of the lungs, in which the human development has simulated that of some of the lower animals, where the pleural cavities are connected; and (f) some violent exertion, *e.g.*, coughing, sneezing, physical strain and, rarely, trauma.

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PAPILLARY SQUAMOUS-CELL EPITHELIOMA OF THE RENAL PELVIS*

By ALEX. STRASBERG

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THERE is no justification for this report other than the relative infrequency of the condition described. Tumours of the renal pelvis constitute 0.025 to 0.1 per cent of all tumours. All neoplasms of epithelial origin are epitheliomata. There is a further sub-division into squamous-cell, transitional, sessile, etc., depending on cell predominance and cellular differentiation.

For clinical purposes the recognition of two types, the papillary and the non-papillary will be sufficient. Hæmaturia, intermittent or constant, is characteristic of the former. It occurred in all of Hunt's¹ 15 cases. In only 4 of his patients was a palpable mass felt; this however is more constant in the non-papillary form (squamous-cell epithelioma), *vide* cases recorded by Silverstone,² Priestley.³ One can appreciate the significance of the tumour mass when one considers the intimate association that exists between the non-papillary tumour, stone, infection, and hydronephrosis. From the primary focus in the pelvis the non-papillary growth extends into the perirenal tissues, where-

as the papillary tumour transplants its nidus into the ureter or bladder. The presence of a papillomatous growth in the bladder should make one suspicious of a parent lesion in the ureter or pelvis.

The genuine papillary growth originates, develops and concentrates on the complete destruction of the renal pelvis and calyces before it seeks virgin fields. The non-papillary tumour is accepted as the more malignant grade, and ordinary nephrectomy is advocated, whereas for the moderately malignant papillary tumour nephro-uretero-cystectomy (segmental) is recommended as the procedure of choice. Priestley says "The prognosis is extremely poor in the non-papillary tumours."

Prevalence.—Papillary epithelioma is commoner in the male than the female. The average age which it affects is 52 years. The literature on papillary epithelioma of the renal pelvis records 15 cases by Hunt from the Mayo clinic. Joelyn Swan⁴ has communicated 2 from a series of 65 new growths of the kidney. Cabot and Allen⁵ report 24 papillary tumours in a group of 27 malignant renal pelvic tumours. (Some of these were previously reported by Hunt). From the largest recorded group of 337 cases

* From the Urological Service, Jewish General Hospital, Montreal.

of tumours of the renal pelvis, Swift-Joly⁶ has classified 138 papillary carcinoma.

Etiology.—The presence of stone and infection in the larger number of the squamous-type tumours implicates them as contributing causes, but however not in all tumours do we find calculi or infection. Moreover many patients with calculosis, chronic pyelitis, and renal tuberculosis never develop malignancy.

Prognosis.—This is poor in both types. Cabot and Allen seem to favour the papillary form, the duration of life after operation being three years on the average.

CASE REPORT

S.G., male, married, aged 34, was admitted to the Jewish General Hospital on April 27, 1936. He had always enjoyed good health except for an appendectomy in 1930. One day in August, 1935, following a routine day's work he voided bloody urine, both fresh and clotted. There were no other urological symptoms. He was perfectly well again until December, 1935,

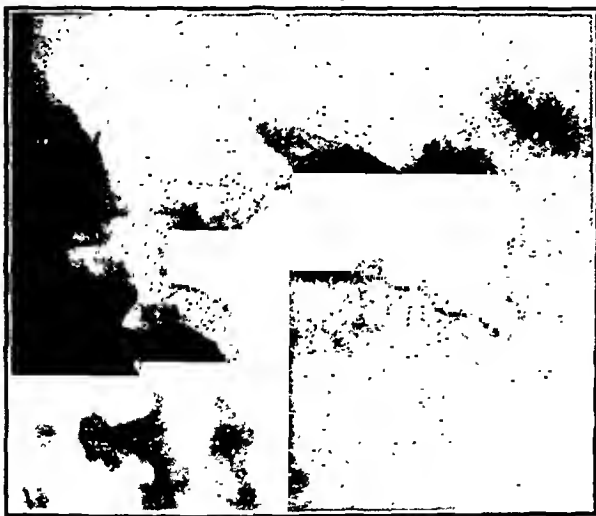


Fig. 1

when an attack of hæmaturia was preceded by localized pain in the left loin. Two weeks prior to admission this pain became constant in character. There was no loss of weight but "his 'pep' was not what it used to be", as he himself put it.

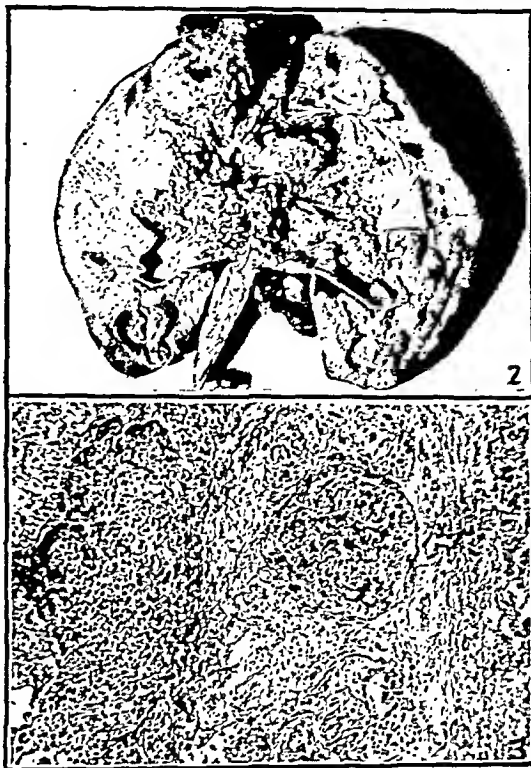
Physical examination was essentially negative, except for tenderness in the left loin and left upper quadrant of the abdomen. The kidneys were not palpable and no mass was felt.

Laboratory findings.—Urine: acid, turbid; specific gravity 1.010; albumin +; sugar 0; erythrocytes, plus 2; scattered pus cells; epithelium, present. Phenolsulphonphthalein, 1st hour 40 per cent; 2nd hour 10 per cent. Non-protein nitrogen, 15.5 mg. per cent; creatinine 1.44 per cent.

The Wassermann test was negative. Leucocytes, 10,300. The sedimentation rate was markedly increased; moderate leucocytosis with neutrophilia, lymphocytosis, monocytosis and a moderate shift of the polymorphonuclears towards immature forms, suggesting malignancy or a severe chronic infection.

Cystoscopy.—The bladder mucosa was normal; no blood seen oozing from either ureteral orifice; catheter-

ization of both ureters encountered no obstruction. The specimens of urine were normal except for a preponderance of erythrocytes from the left kidney; the urea N. was equal for both sides. Sodium iodide was injected into each pelvis. The right ureter and pelvis were practically normal; the left renal pelvis failed to fill even though a greater amount of dye was



directed there. Intravenous urography still showed rather poor filling on the left side. The pelvis appeared to be deformed, and only the lower third filled; there is a suggestion of pressure from above causing this deformity. A roentgenogram of the chest was negative. A diagnosis of malignant renal tumour was made, and it was decided to operate. The patient was re-admitted on June 17, 1936. In the interval he had arranged his business and was receiving deep x-ray therapy. The urine was packed with erythrocytes. Another uroselectan series showed a similar picture as the last.

Nephrectomy was done on June 17, 1936. Under avertin, gas and ether the kidney was exposed through the usual loin incision, the 12th rib being resected because of the high position of the kidney, which was also enlarged and covered with distended vessels. It was very adherent, and extirpation was attended with considerable bleeding. The pedicle was large and surrounded by several glands. An iodoform drain was left in and the wound closed in several layers. Intravenous glucose, 10 per cent, was administered while the patient was still on the operating table, and a blood transfusion was given within the next 24 hours. Convalescence was uneventful, and the patient was discharged on July 13, 1937, with a small sinus in the wound. He was to report later for further deep x-ray therapy.

Pathological diagnosis.—Kidney measured 12 x 6 x 4. In the region of the hilus there was a hard mass which measured about 2 x 3. On section the pelvis was dilated and occupied by warty masses. The calyces were irregular and eroded, and the whole pelvis was covered with large and small papillomatous masses. The ureter was not involved. The paren-

chyma is thinned out, down in the upper and mid-region. Microscopically, there was slight diffuse round-cell infiltration and an occasional clump of tumour cells. At one place the kidney parenchyma was entirely replaced by tumour, which was largely made up of thin vascular septa supporting layers of transitional and squamous epithelium growing in large papillary formations. In other places it was made of solid nests of squamous cells. There was a tendency towards "pearl" formation. (Dr. D. Seecef)

Diagnosis.—Papillary transitional and squamous-cell epithelioma of the pelvis of the kidney with extension into the kidney.

About two months later patient was re-admitted complaining of pain in the left loin and lower quadrant of abdomen, anorexia, loss of weight, and fever in the afternoon. Examination revealed an erythematous area about the scar (x-ray burn), tenderness in the left loin, with a suggestion of deep fluctuation over this area. Exploration of the loin disclosed a large cavity filled with old blood which was evacuated. With the finger in cavity one got the impression of a hard infiltrating mass recurring locally. A specimen of the growth verified this finding. A roentgenogram of the chest showed metastasis to the lungs. The patient died on November 20, 1936, of bronchopneumonia.

Necropsy findings (papillary carcinoma of the pelvis left kidney).—Extension into the retro-peritoneal tissues and perforation of the flank; metastasis to regional lymph nodes, lungs, heart, and right kidney; adhesions to diaphragm; hypostatic pneumonia.

SUMMARY

A case is presented of papillary squamous-cell epithelioma of the renal pelvis.

Gross hæmaturia and a deformed renal pelvis as shown by the pyelogram were the incriminating evidences of renal malignancy.

The tumour was a variable one—squamous and transitional layers in papillary formation, and solid nests of squamous cells in bands of fibrous tissue.

Extension was into the kidney parenchyma, and at necropsy the opposite kidney was involved.

There was no metastasis into the ureters and bladder. The pronounced malignancy is more typical of the non-papillary squamous-cell epitheliomata.

I am indebted to Dr. Max Ratner, Chief of Service, for valuable assistance.

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Case Reports

A CASE OF UNUSUAL CALCIUM DEPOSITION DUE TO RAYNAUD'S DISEASE

By C. J. HOUSTON, Yorkton, Sask. AND
E. JOHNSON, Selkirk, Man.

Miss J.L., aged 21, a student in Manitoba University, came to one of us in May, 1935, complaining of painful nodules in the fingers. She had been aware of some distortion in the shape of her fingers for years. Some two years previously her hand had been x-rayed as an experiment in her work in the Physics Laboratory in the University. Peculiar deposits were then noted in the soft tissues of the finger tips of both hands (see Fig.).

When questioned about circulatory disturbances she stated that she had frequent spells of pallor and numbness of both hands, with weakness and stiffness of the fingers and decreased skin temperature. The lower limbs were not affected. These attacks occurred at irregular intervals, and the duration would be five to fifty minutes. They were brought on chiefly by exposure to cold, excitement, or other form of nervous tension. For example, in writing examinations she often had to wait ten minutes before her hands would relax sufficiently to permit of using her pen.

Her previous history was negative, except that her dentist had told her she had insufficient calcium in her teeth.

Both parents showed some disturbance of the autonomic nervous system, chiefly functional digestive disorders.

Examination showed numerous hard nodules in the soft tissues of the fingers. No similar deposits could be found elsewhere in the body. X-rays of lung and kidney areas revealed no other areas of abnormal calcification. The blood Wassermann test was negative.



Tuberculous disease was ruled out. A specimen of paste removed from one nodule was analyzed and contained calcium. The blood calcium estimation was within normal limits (10.9 mg. per 100 c.c. blood). We felt that the condition was not due to any dysfunction of general calcium metabolism. A diagnosis of Raynaud's disease was then made. A similar case has been reported by Watson-Jones and Roberts.¹

This unusual manifestation of Raynaud's disease is particularly interesting in that it illustrates one phase of Leriche and Policard's theory of ossification and calcification. Briefly this may be outlined as follows.

There is normally a balance between the calcium content and the vascularity of mesenchymatous tissue (which is probably associated with phosphatase activity).

1. In the case of bone a normal circulation results in normal calcification; an increased blood supply causes decalcification; a decreased blood supply produces increased calcification. If the blood supply is cut off calcification remains unchanged.

2. In any mesenchymatous tissue of low metabolism a decreased blood supply results in pathological calcification, as when it follows fibrosis, trauma or infection.

In the case presented it is apparent that the frequent though transient limitation of blood supply produced by Raynaud's disease has resulted in such a pathological calcification.

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AN UNUSUAL HEAD INJURY

By CHAS. K. FULLER, F.R.C.S.(C.&E.)

Yarmouth, N.S.

Correctly or incorrectly, in my diagnosis and prognosis of head injuries I have always considered that if the contents of the cranial cavity had been injured such injury would show itself by a period of loss of consciousness, and if by any chance this loss of consciousness was so transitory as to be unnoticed it in turn would reveal its presence by the fact that the patient vomited. For over twenty years I have always found this simple rule to be very reliable. In particular, the significance of vomiting has sometimes saved me from grave prognostic errors in injuries that on the surface seemed rather trivial. Any case which in its inception or course upsets the usually accepted standards would seem to be worthy of more than passing notice.

CASE REPORT

On December 21, 1937, E.A., a healthy male, forty-nine years old, while working as a longshoreman, was accidentally struck a hefty blow by a hoisting hook over the left eyebrow. He felt somewhat faint, the skin was broken and the eye blackened. The open wound

became badly infected but with anti-streptococcic medication (streptocide) and usual care, after a somewhat strenuous time it eventually cleared up, and in two weeks the patient was around apparently as well as usual.

On January 24, 1938, five weeks after his accident, the patient was admitted to my service in the Yarmouth Hospital, complaining of headache and incontinence of urine and faeces. Physical examination gave little additional information.

He was a well nourished out-of-doors type of man. The blood pressure was 100/30. Pulse slow 50 to 60 and soft. Temperature normal. It is difficult to describe his mental state. He seemed perfectly rational and keen but with it showed an apathy that was more than apathy, a man tired in both body and soul. The reflexes were somewhat depressed; the sensory normal or slightly dulled. The muscles showed spasticity with some slight myasthenia but were otherwise normal. He had loss of bladder control, and loss of sexual characteristics. Otherwise the genito-urinary system was normal. Appetite was fair but he had loss of control of defaecation. The hearing was normal. The pupils were equal and normal in size, reacting to light and accommodation. Vision was normal in both eyes. There was a small scar in the middle of the left eyebrow which is not tender. Eye grounds both normal in all respects. No congestion or choked disc.

An x-ray examination of his head showed a most unexpected condition. The hook, penetrating and fracturing the roof of the orbit, had torn through the frontal sinus and fractured its posterior wall in such a way that a fragment over an inch in diameter had been driven through the frontal lobe of the brain and had penetrated the left lateral ventricle. In addition, this fragment had assumed such a position that it formed a connection between the cavity of the frontal sinus and the ventricle and acting as a valve the ventricular system was pumped completely full of air displacing all the cerebrospinal fluid.

Here then was a foreign body, approximately an inch in diameter and three-sixteenths of an inch thick, embedded in the frontal lobe, apparently part of a fistula between the ventricle and the nasal cavity in an area which but three weeks before had been the scene of a violent inflammation. Any surgical procedure must allow of closing the fistula, removing the foreign body, give sufficient room to handle any emergency that might arise, especially haemorrhage, and yet must disturb as little as possible any existing adhesions and scar tissue.

With these considerations in view, under local anaesthesia (5 c.c. adrocaine) an incision was made throughout the length of the left eyebrow right down through the periosteum and the anterior wall of the frontal sinus exposed. The sinus was entered at its lateral extremity through the anterior wall which proved to be unusually thick, about one-quarter of an inch, and exceedingly hard. The opening was enlarged laterally, i.e., into the anterior cranial fossa to the extent shown in the x-ray picture to give sufficient room to work and to allow of the fistula and fragment being approached by the shortest route. The opening of the frontal sinus into the nose was identified, closed and packed off with gauze moistened in bismuth and iodoform paste. The fractured roof of the orbit was identified and cleared of adhesions over a width of a little more than an inch to its posterior border which, as the pictures show, led directly to the superior edge of the embedded fragment. This was seized, to steady it, cleared of adhesions and extracted. There was no haemorrhage and practically no loss of cerebral tissue. The posterior portion of the orbital roof was identified and pressed back into position followed by the anterior. The rent in the dura mater was so awkwardly placed that it could not very well be sutured, so the wound was packed with gauze moistened with bismuth and iodoform paste and the skin with subcutaneous tissue closed with interrupted sutures. While the operative opening may be large enough to be a potential source of danger it can very easily be

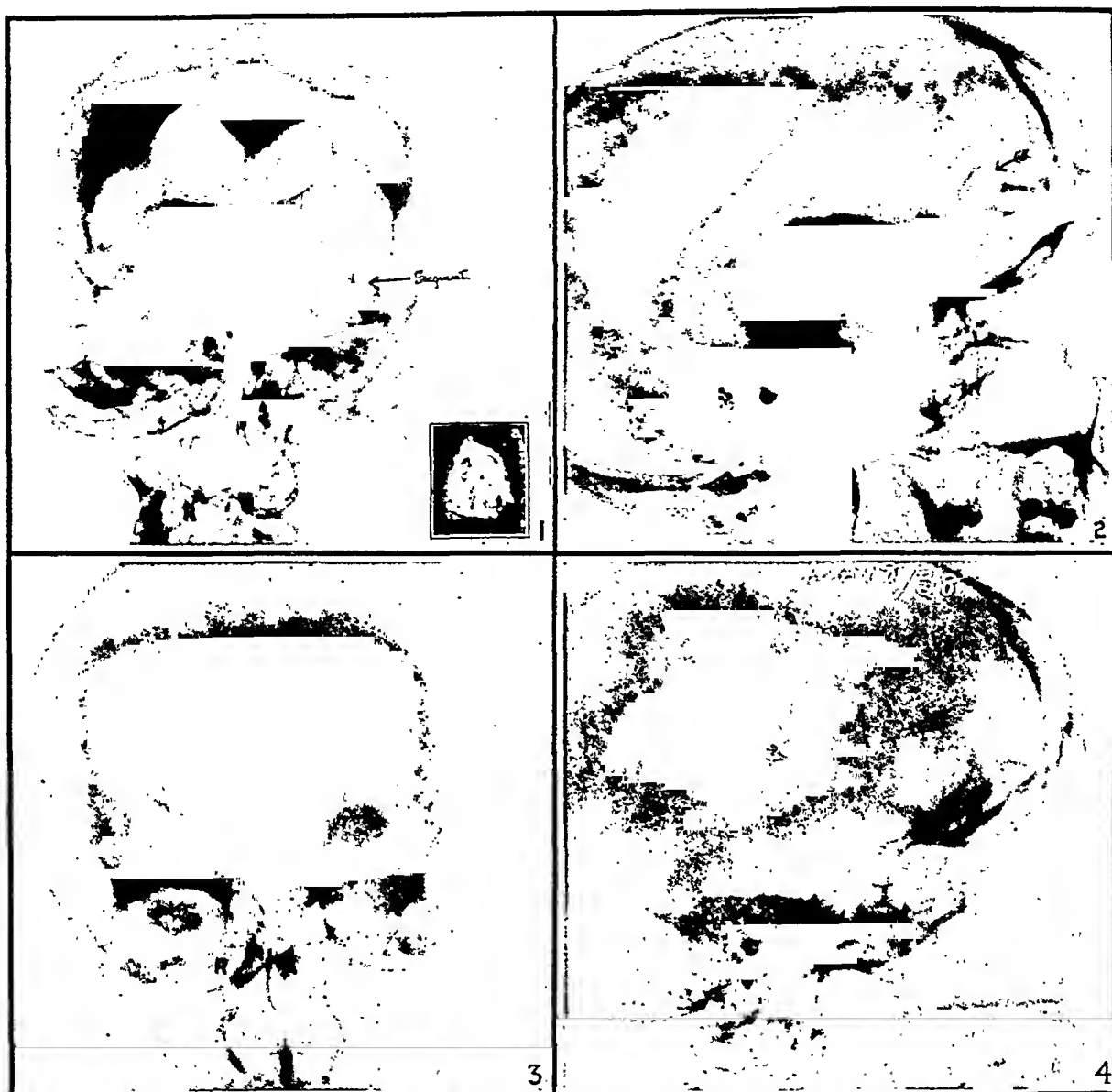


Fig. 1.—Antero-posterior view before operation showing the ventricles distended with air by valve-like action of fragment. (a) Fragment, reduced 58 1/3 per cent from original size. Fig. 2.—Lateral view before operation showing fragment embedded in frontal lobe, the fractured roof of orbit, and distended ventricles. Fig. 3.—Antero-posterior view three weeks after operation, showing normal conditions. Fig. 4.—Lateral view three weeks after operation showing normal condition of ventricles.

covered with a plate at a later date without danger to the patient.

He was given 5 gr. of streptocide three times a day for five days, and on the second day foreign protein (5 c.c. boiled milk) was given intramuscularly.

His recovery, while in no way spectacular, was intensely interesting to watch. Within twenty-four hours his general appearance changed for the better and his headache disappeared. On the second day he was somewhat restless, picking at the bed clothes and his bandages, although on enquiry he said he was perfectly comfortable. This continued for four days and he required a mild sedative each night to ensure sleep. By the fourth day his involuntary defecations ceased and he became constipated, but there were no bladder sensation until the sixth day and function was not fully restored before the twelfth. Daily x-ray pictures were taken but there was no appreciable change in the condition of his ventricles until the sixth day. On the twelfth day when bladder function was restored and he seemed perfectly normal very little air remained, as can be seen from the pictures.

Several features of this unusual case seem worthy of comment. In the first place, despite the magnitude of the intracranial lesion, if there was any loss of consciousness at the time of injury it must have been very transitory and unnoticed; certainly the patient never vomited. Then again, although air must have displaced the spinal fluid for some time, probably weeks, the first symptom outside of a moderate headache was loss of bladder control, rapidly followed by loss of bowel control, and even after these had appeared, outside of his general appearance, examination revealed the only deviation from the normal in the other systems to be a slowness of response. Mentally, in talking

with the patient before and after his operation, he seemed perfectly normal, though apathetic, could and did answer all questions intelligently but now has absolutely no memory of anything from about two weeks before his admission to the hospital until the night he wished to urinate six days after his operation. He does not remember leaving home some sixty miles away and coming to hospital, nor can he recall ever having seen me before the sixth day after his operation. His memory of events since that time is perfectly clear. In conclusion, one cannot help but meditate as to just how great was the rôle played by anti-streptococcic medication (aminosulphamide) in preventing such complications as meningitis or cerebritis.

CONGENITAL RHABDOMYOMA OF THE HEART*

By M. VIOLA RAE, M.D.

Toronto

Baby O K., a male of 9 pounds 1½ ounces, delivered normally at term, was admitted to the Hospital for Sick Children on November 20, 1936, at the age of 2 days with a history of attacks of cyanosis developing 10 hours after birth. There had been no difficulty in resuscitation at birth and the child cried lustily. The first attack lasted 1 hour and gradually cleared, but subsequent attacks increased in duration and frequency until at 2 days of age the cyanosis was persistent and generalized. The skin was mottled and the lips cyanosed. Respiration was distressed, rapid and grunting. The chest was large, symmetrical and barrel-shaped. The breath sounds were vesicular, with a few râles over both bases. The area of præcordial dullness was markedly enlarged, extending from the right nipple line to the left lateral chest wall, and from the clavicle to the area of liver dullness. Heart sounds were muffled and indistinct but no murmurs were heard. The heart rate was very rapid and no irregularity was noted clinically, although electrocardiographic tracings were not made. The liver was enlarged almost to the level of the umbilicus; the spleen was also enlarged to 2 finger-breadths below the costal margin. The cyanosis steadily progressed in the oxygen tent and the child died on its third day. X-ray showed an abnormally large heart shadow occupying the major part of the thorax. Red blood cells 6,000,000; white blood cells 19,000; hgb. 120 per cent; calcium 9.03 mg.

Autopsy was performed 12 hours after death. The anatomical diagnoses were: (1) congenital rhabdomyoma of heart; (2) patent foramen ovale and ductus arteriosus; (3) partial atelectasis; (4) hydropericardium; (5) hepatomegaly; (6) splenomegaly.

Over one-half of the thorax was occupied by a tremendously enlarged heart and pericardial sac. The pericardial fluid was excessive, amounting to about 15 c.c. The heart was roughly globular in shape measuring 7 cm. in diameter. A few small circumscribed greyish pink nodules, measuring from 0.5 to 1 cm. in diameter, were visible through the pericardium in the apical region of the left ventricle and also in the auricular walls. On opening the heart a thick distorted inter-

ventricular septum was found bulging into both right and left ventricles. In the right ventricle the septal surface was nodular and warty, projecting into the cavity, which was almost obliterated. The septum was incised longitudinally and a large, round, circumscribed tumour mass was exposed, measuring 4.5 cm. in diameter and surrounded by only a narrow rim of compressed myocardium (Fig. 1). The tumour was clearly demarcated from the muscle by a fine capsule. The cut surface was uniform, soft, moist, putty-like, pinkish grey in colour and everted slightly above the cut edge. Besides the large tumour in the septum, multiple smaller nodules were present. Two nodules, each measuring 1 cm. in diameter lay in the left ventricular wall near the apex; another 0.7 cm. in the right ventricular wall near the base and two 0.5 cm. in the right auricle. The small nodules were similar to the large mass on cut surface. The valve leaflets were thin and pliable and were not involved in the tumours. A small foramen ovale still remained and the ductus arteriosus was patent. The great vessels arose in the usual manner and appeared normal.

The lungs were partially atelectatic in their lower lobes; the liver and spleen were enlarged and congested. Small deposits of uric acid crystals lay in the medulla of the kidneys. Other organs appeared normal.

Microscopic examination.—Sections from various tumour nodules all showed a similar histological picture. They were enclosed with a thin fibrous capsule for the most part, but here and there the tumour cells had broken through and lay adjacent to the muscle cells. The tumour cells had a peculiar lacy appearance due to the presence of large irregular vacuoles. Individual cells were extremely large, many of them approximately the size of a fetal glomerulus. A wide variety of bizarre cells of embryonic character constituted the tumour and no uniformity of type cell could be identified. In shape they were found round, oval or spindle-shaped, with nuclei central, eccentric or compressed to the peripheral cell membrane. The nuclei were large or small, pale or hyperchromatic, many with prominent nucleoli, often vesicular. Many cells showed a centrally placed nucleus about which the cytoplasm was arranged in fine radiating acidophilic fibrils extending toward the periphery, forming the spider cells so characteristic of rhabdomyoma. A few cells contained a diffuse, granular, pink-staining cytoplasm suggesting ground glass. Under very high power many of these cells showed the finely granular structure arranged to form vague cross-striations suggesting those of a striated muscle cell. This character was more clearly elicited with phosphotungstic-acid-haematoxylin stain. Much distortion of cells existed due to large clear vacuoles occupying the main part of the cytoplasm and displacing the nucleus. Many large clearly outlined spaces bore no relation to neighbouring cells and were devoid of nuclear or any stainable material. The contents of these vacuoles could not be determined. In paraffin preparations the vacuoles were empty and clearly defined. Frozen sections stained with Sudan III showed no evidence of true fat within the vacuole, but a few very tiny droplets lay within the cytoplasm of the cell. Mitotic figures and multinucleated cells were not found. Small thin-walled blood vessels were present in moderate numbers. A few fine strands of supporting stroma were interspersed between large groups of tumour cells.

COMMENTS AND CONCLUSIONS

Rhabdomyoma of the heart forms a small group of the many deformities which are present at birth. The important factors in relation to myocardial function are the size of the tumour and its location as related to the conducting mechanism of the heart. The invasive quality of the tumour appears to be practically

* From the Department of Pathology, Hospital for Sick Children, Toronto.

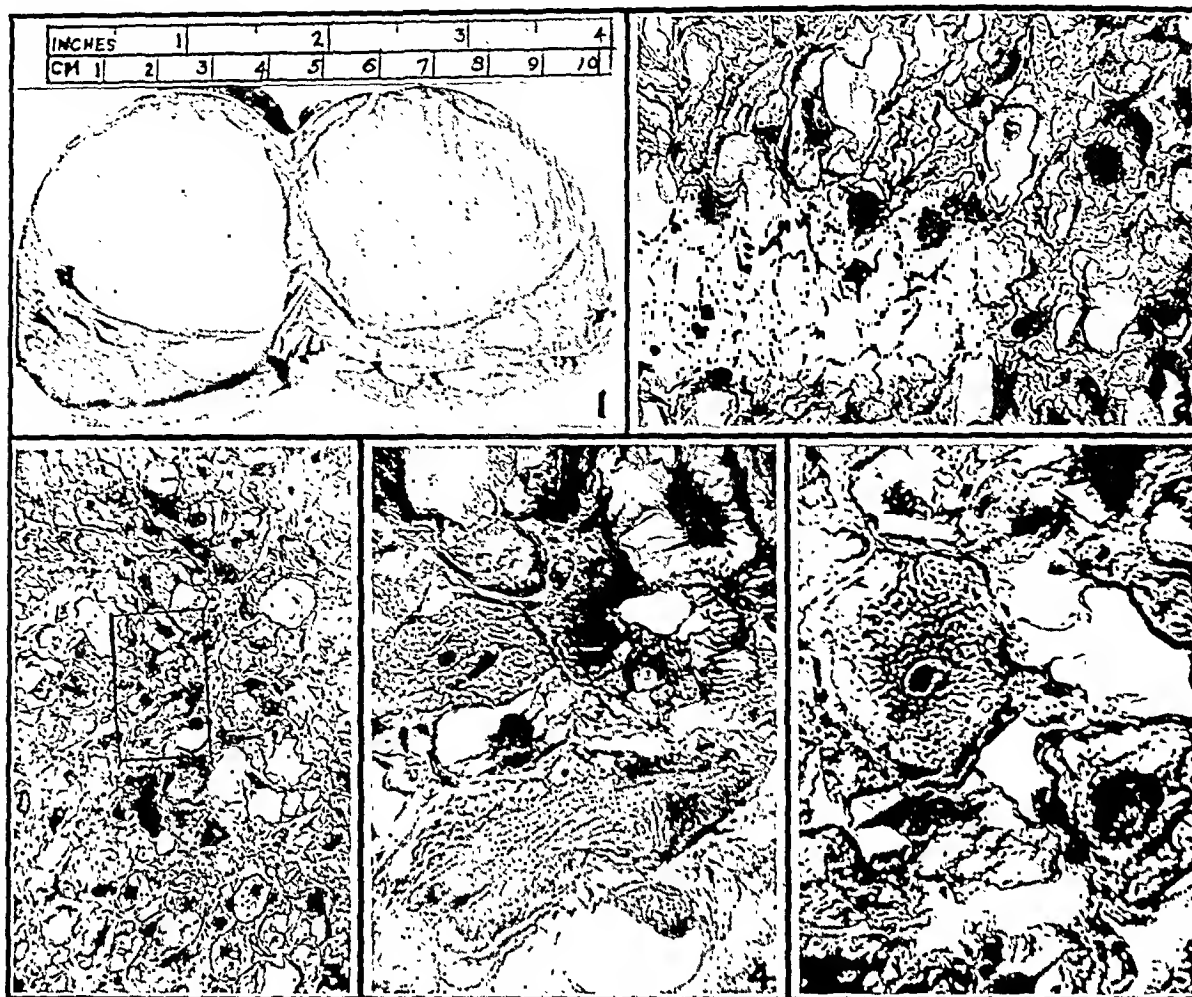


Fig. 1.—Large rhabdomyoma occupying interventricular septum, with smaller tumours nearby. Fig. 2.—Laey appearance of tumour cells. (P.T.A. x 150). Fig. 3.—Cellular structure of rhabdomyoma. (P.T.A. stain x 100). Fig. 4.—Tumour cell showing longitudinal and cross striations. Other vacuolated cells. (P.T.A. x 600). Fig. 5.—“Spider cell”. (P.T.A. x 600).

nil. Pressure and distortion however, interfering with contraction of the muscle fibres as well as conduction of impulses are of greater moment. Although the tumours are not considered genetically related to the Purkinje cells, but rather to the pure muscle cells (Hueper), it is unlikely that conduction could remain undisturbed in proximity to a tumour of such dimensions as the above.

This case of rhabdomyoma adds one more to the relatively small number in the literature (49). The salient features of the case are the multiplicity of tumours in the myocardium (6),

the remarkable size of the mass in the septum, the associated large liver and spleen, and the embryonic type of cell with the lack of malignant histological characters.

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OPHTHALMIC INDICATIONS FOR ABORTION. — A. Favory is of the opinion that pregnancy should always be terminated in the presence of retinitis of renal origin; not only the possibility of blindness but also the condition of the kidneys are the deciding factors. In retrobulbar neuritis, syphilis and nasopharyngeal conditions having been eliminated, induction should be considered. Myopia is often aggravated by pregnancy, and in these cases retinal hemorrhages and

detachment sometimes occur. Pregnancy should be forbidden where there is already detachment in one eye. All forms of choroiditis, uveitis, and keratoconus are made worse; in the first of these abortion should be considered. In hereditary types of eye disease which may involve blindness the necessity for intervention is not yet generally admitted. Here the eugenic and legal aspects of the case must influence the decision.—*Progr. med.*, Paris, January 29, 1938, p. 153. Abs. in *Brit. M. J.*

Therapeutics and Pharmacology

SULPHANILAMIDE IN GENITO-URINARY INFECTIONS.

BY N. E. BERRY

Kingston, Ont.

In no field of modern therapeutics have there been such real advances as in the chemotherapy of chronic urinary infections. The introduction of the ketogenic diet, followed in 1936 by the development of an exogenous agent, mandelic acid, practically revolutionized the whole subject and gave us a far more effective agent than we had ever had before. Then in July, 1937, Kenny published the first series of cases treated by sulphanilamide with results that were striking. Since then the application of this drug has steadily increased until at the present time its fame has reached the laity. Being introduced under such circumstances and with such enthusiasm it is not easy to evaluate its real worth.

Already sufficient data have accumulated to prove beyond question that sulphanilamide is of very great value in urinary infections, and compares favourably with its nearest competitor, mandelic acid. Generally speaking, I think it is admitted that it is equally efficacious in that large group of coli infections which comprise the great majority of all cases. It is also useful in *B. proteus* infection and in some coccal infections in which mandelic acid is of no value.

From the point of view of administration sulphanilamide has definite advantages. It is cheaper, it is easier to take and does not require the limitation of fluids and careful check of the acidity of the urine which is essential to successful use of mandelic acid. Further, since it is cheap and effective in more than one type of organism, the practitioner may well use it where he has not the facilities for making proper bacteriological studies. On the other hand, sulphanilamide is by no means an innocuous drug. Its administration is usually accompanied by some digestive disturbance or malaise, and, at times, by alarming symptoms, which are well known. The newer mandelic acid preparations are becoming cheaper and more pleasant to take. They will, therefore, hold their place. Undoubtedly certain strains of organisms which are resistant to one of these drugs may respond to the other, so that where one fails the other should certainly be tried.

Largely due to a highly promising report of a small series of cases published by Dees and Colston sulphanilamide has been enthusiastically taken up as a cure for gonorrhœa and published reports claim almost uniformly successful results. The only disturbing publica-

tion is that of the Therapeutic Trials Committee of the Medical Research Council. In a report published in the *British Medical Journal*, September, 1937, they give their opinion that the drug is of little value.

In trying to evaluate any method of treatment of such an unsatisfactory disease one must first of all remember that the disease will get well of its own accord in an appreciable number of cases within a month, provided the urethral mucous membrane is not unduly irritated. This fact is made use of both by the profession and by manufacturers of patent medicines. Secondly, too many men assume that a patient who does not come back means a cure—it is more likely the patient is worse and has gone elsewhere. I am convinced that these two considerations are responsible for mistaken appreciation of the real value of any treatment. I cannot deny that in some cases the discharge clears up in a spectacular way following the administration of sulphanilamide, but it rarely remains so, and in a little while it comes back as bad as before. A second course of treatment frequently gives no results.

I have had the opportunity of studying approximately 50 acute cases in hospital. I have seen ordinary cases under hospital conditions put on sulphanilamide and run the whole gamut of complications. I cannot agree, therefore, that this method of treatment lessens the likelihood of complications. In cooperation with Capt. Sutherland, I have also followed the cases in the District Military Hospital. It was found that the average stay of patients in hospital was not lessened when they were given sulphanilamide alone as compared with local treatment alone.

From these experiences it is my conclusion that sulphanilamide cannot be relied upon to consistently give the spectacular result that reports hitherto would indicate. In speaking to practitioners throughout the district, I also note a change in general opinion. Six months ago they were uniformly optimistic. Today many admit discouraging results. I do not suggest the drug is of no value and should be discarded: I do suggest that its efficacy in the treatment of gonorrhœa has been greatly over-estimated; that it is not nearly as efficient here as in kidney infections, and one must particularly caution against using it without properly examining his patients. Certainly you cannot expect results in cases with a stricture of the meatus or similar obstructive factors. Sulphanilamide is not the panacea we have been hoping for, and for the present we shall have to continue our local treatment, which has none of the glamour of the hypodermic needle or the appeal of the pill.

In the first cases treated large doses were given for two days and then gradually reduced to a maintenance level. I cannot see that there is any real advantage in this, and at present I employ a dosage of thirty to fifty grains a day. This is approximately the same as Colston has used in the last series he reports. In giving patients the drug it is most important to be sure that they will not have enough to take it more than a week without coming back for observation. Prolonged use without such observation is extremely dangerous.

THE MANAGEMENT OF THE PREMATURE INFANT

BY HOWARD MCGARRY, M.D.

Niagara Falls, Ont.

An infant, whether of a single or multiple pregnancy, weighing under five pounds should always be considered as premature and treated as such. The three axioms in the care of premature children are (1) to maintain normal body temperature; (2) to feed them properly; and (3) to prevent infection.

To maintain normal temperature in the hospital is comparatively simple as a premature room is usually available. This should be kept at between 80 and 95° F. temperature and a humidity of 55 per cent. The construction of the premature room will not be discussed here, but the above two points should be watched closely. The temperature of the infant should be taken every four hours, and maintained at 98 to 100° by varying the temperature of the room. It is most important that the body temperature does not drop to subnormal, for if the infant becomes chilled it is most difficult to elevate the temperature again.

If the premature infant is born in the home the doctor often wraps the baby in wool and sends it to the hospital. This is not sufficient, as a premature child produces very little heat, and unless supplied with adequate external heat will arrive at the hospital with a subnormal temperature. The prognosis in these cases is 75 per cent poorer than in those born in hospital and immediately moved to the premature room. If the infant is to be cared for in the home a basket nest may be simply constructed. The temperature of the room should be increased and the basket temperature increased with hot water bottles. The temperature of the thermometer next to the blanket in which the baby is wrapped is read every two hours instead of disturbing him to take his temperature rectally. The body temperature however must be taken at least four times in every twenty-four hours. The construction of the bed and clothing for premature infants may be obtained from any good textbook. To sum up, the body temperature of premature children must be maintained by rigid control of external heat.

It is impossible to over-estimate the danger to the premature from contact with anyone who has a cold or sore throat. A premature infant who contracts pneumonia dies, while even a simple cold is accompanied by grave danger. Suffice it to say, guard the infant from contact with infected articles or persons.

The feeding is started from 6 to 8 hours after birth. Breast milk should be obtained by pumping either from the mother or, if the mother has no supply, from some other source. There is no substitute for breast milk. A mixture of breast milk and full strength protein milk is best. Use 2/3 breast milk to 1/3 protein, *e.g.*, breast milk 6 ozs., protein milk 3 ozs. The purpose of the protein milk is to make the feeding more constipating. Start with 1/2 oz. every 3 hours. Increase one dram per feeding as the infant's tolerance increases, up to requirements (60 to 70 calories per pound). If the mother has breast milk her infant may nurse when 5 lbs. If not, this feeding may be substituted—butter soup 20 ozs.; protein milk 10 ozs. Feeding as above. When the infant reaches 7 to 8 pounds this may be changed to any of a number of formulæ, the best of which is cultured lactic acid milk and corn syrup. However, almost any standard formula will be satisfactory. Premature infants are born with an iron and calcium deficiency. At four to six weeks the iron can be added in a form of iron ammonium citrate. Start with grs. xv in the whole day's feeding, and gradually increase to 40 or 60 grains daily. Viosterol or percomorph oil, 3 drops, twice a day, should be given along with the iron.

If breast milk cannot be obtained start with 1/2 strength S.M.A.P., gradually increasing to full strength. The other feeding steps are the same as above. This latter feeding is safe, but the infants will not gain so rapidly as on breast milk.

Premature infants are especially prone to gastro-intestinal disturbances. One loose stool is of great significance and should always be brought to the attention of the physician, so that prompt feeding adjustment can be made. Plain boiled water is given between feedings, and if the infant becomes dehydrated 5 per cent lactose water in as large quantities as the infant will tolerate. Interstitial injections of 5 per cent glucose are given only as a last resort.

The method of feeding depends upon the vitality of the infant. As a general rule the Breek feeder will suffice for the great majority and should be used until the infant is five pounds. If very weak, use the gavage or drop-per method. After five pounds is reached the standard infant feeding bottles and nipples may be used. For the drowsy premature infant occasional flicking of the feet with a finger sufficient to make him ery is beneficial and should be a routine procedure.

Editorial

THE ETIOLOGY OF APPENDICITIS

THE question may be asked: Why take up time and energy in discussing such a threadbare subject as appendicitis? Since Fitz¹ published his classical monograph which differentiated "appendicitis" from "perityphlitis", "typhlitis", and "inflammation of the bowels" many years have elapsed, and we have seen the disease pass from a novelty to a fashionable ailment, to a widespread menace. Yet in spite of better diagnosis and improved surgical technique the mortality from appendicitis is not decreasing. It is evident that the last word has not been said. Both from the clinical and experimental sides the condition presents a problem which, from the point of view of etiology and pathogenesis, at least, is still involved and unsolved. It would not seem, therefore, a useless task to review the subject once again in the hope of getting new light.

On looking over the literature one gets the impression that diametrically opposed views are expressed over what appear to be the simplest matters—for example, the infective agent, its nature, or, indeed, whether there is an infective agent at work at all; if an infective agent is responsible, where does it come from?; is a solution of continuity of the mucosa of the appendix necessary?; in how far is obstruction of the lumen important?; what part do fecoliths and other foreign bodies play?; are disturbances of the circulation of blood and lymph etiological factors? There are several reasons, possibly, why differences of opinion exist. It is rare to get for study an appendix which exhibits the first stage in the inflammation, and at any stage the finer histological appearances may be distorted by the operative manipulation. It is therefore difficult to trace the sequence of events. Experiments conducted on animals are not strictly comparable with the natural experiments

that take place in man. Where, too, as here, a number of different factors enter into a problem it is difficult to decide which are predisposing and which exciting and to assess the relative importance of each. Such matters come into mind here as the anatomical structure of the appendix; its position; its relation to other organs; its circulatory apparatus; its nervous mechanism; peristalsis; obstruction of the lumen from kinking or foreign bodies; mechanical damage to the mucosa; trauma; impeded circulation and bacterial insults; the nature of its bacterial content; its "remote control", so to speak, by distant foci of infection; and, of course, allergy. All of which emphasizes that the subject of appendicitis is by no means simple.

The appendix is relatively rich in lymphoid tissue during the growing period of life, which fact, for certain reasons, would seem to account for the frequency of appendicitis in youth and the early adult period and the relative immunity of the middle-aged and aged. Diverticula are occasionally found, and Chase, of Montreal, is of the opinion that, like diverticula elsewhere in the intestine, these conduce to an inflammation which may last months or years and then terminate suddenly and unexpectedly in perforation.

The appendix may be found in various positions, determined by its original anatomical relations and by other accessory facts, such as its length and that of the meso-appendix, intestinal contents, abdominal pressure, pelvic contents, and abnormal peritoneal adhesions or deformities (Oertel). Accordingly the organ may be directed in various directions, and the tip may touch the ovary or Fallopian tube, the liver, gall bladder, spleen, kidney, stomach, duodeno-jejunal flexure, and the descending colon. When dependent the appendix becomes a ready receptacle for secretion and foreign bodies, the degree of disturbance being in inverse proportion to the efficacy of peristalsis; when out of position it may become

1. FITZ, R. H.: Perforating inflammation of the vermiform appendix: with special reference to diagnosis and treatment, *Trans. Ass. Am. Physicians*, 1886, 1: 107.

kinked, with all that implies, retention of its contents and disturbance of its circulation. There is little doubt that adhesions about the appendix, by causing deformities, traction, and kinking, predispose to acute attacks or exacerbations of appendicitis.

The circulation in the appendix is peculiar in that the blood-vessels are isolated in three zones—the first zone being at the base, where anastomoses are lacking; the second in the centre, with free anastomosis; and the third at the tip, where anastomoses are again lacking. Therefore, kinks at the base of the appendix, the pressure of foreign bodies or exudate, may so interfere with the circulation as to cause stasis, thrombosis or gangrene. One may believe, with reason that some cases of “clinical” appendicitis are not primarily due to inflammation but, rather, to a sudden stoppage of the circulation. The nerve supply is similar to that of other parts of the intestinal tract.

The vast majority of appendicitides are due primarily to infection rather than to vascular disturbances (necrosis; gangrene) which infection is due to the invasion of the organ by bacteria derived from the lumen (enterogenous) or brought to it by the blood (hæmatogenous). Aschoff,² on the basis of extensive studies of the normal and inflamed appendix in man, concluded that the appendix has a special bacterial flora which is responsible for the disturbance that we call appendicitis. He thought, further, that this flora became enhanced in virulence, not because of obstruction of the lumen but probably from stagnation of the fæces within it. He regarded the coexistence of fæcoliths and appendicitis to be fortuitous only, and, indeed, appendicitis can occur in the absence of concretions. Apparently, much depends on the size of the foreign body and the character of its surface. Foreign bodies, if bland, may be present within the appendix without causing trouble. There is, or was before the fire, in the McGill Pathological Museum an appendix full of bird shot. The former owner of the organ had been very fond of game but had never suffered from appendicitis. It would seem logical to suppose that concretions, if large enough, would interfere with the circulation

in the appendiceal mucosa, if pressing, at all events, on those parts where anastomoses are lacking, and, if rough, would cause abrasion of the mucous surface. In either case a solution of continuity in the mucosa could occur, opening up an avenue for the entrance of bacteria.

It seems hardly necessary to invoke a special flora, as Aschoff does, for we know that the ordinary bacteria of the intestine can wreak havoc on occasion. With regard to the question of obstruction, which Aschoff discounts, years ago Macaigne³ showed that *B. coli* derived from the healthy intestine is harmless in the peritoneal cavity but becomes virulent if there is some intestinal disorder, such as diarrhoea, constipation, or *strangulation*. There can be no question, however, as E. W. Archibald, of Montreal, has shown, that perforation of the appendix is more common when concretions are present.

Fischer and Kaiserling,⁴ in order to explain Aschoff's results, suggest that appendicitis is an allergic manifestation, manifested by a specific sensibilization of the lymphatic system which upsets the normal relationship between the appendiceal mucosa and the normal bacterial flora. Controverting this, Heinemann⁵ has shown that the allergic lesions they produced are different from those seen in ordinary appendicitis, the necrosis beginning in the lymphoid follicles rather than in the mucous membrane. She thinks, too, that the pronounced lesions these workers obtained were not due to hypergy but to the toluol which they used as a preservative.

The hypothesis that acute appendicitis was due to the selective affinity of certain throat streptococci for the appendix was advanced by Rosenow. Others (Kretz, Senator, Teale) have expressed similar views. Recently Deaver and Martin⁶ have reported 235 cases of acute appendicitis in children

3. MACAIGNE: Etude sur la néphrite colibacillaire d'origine sanguine, *Arch. gén. de Méd.*, 1896, 2: 722.

4. FISCHER, E. AND KAISERLING, H.: Die experimentelle lymphogene allergisch-hyperergische appendicitis, *Virch. Archiv.*, 1936, 297: 146.

5. HEINEMANN, K.: Zur Frage der allergisch-hyperergischen Appendicitis, *Beitr. z. path. Anat. u. z. allg. Path.*, 1937, 100: 62.

6. DEAVER, J. M. AND MARTIN, A. G.: Acute appendicitis in children, *Surg., Gyn. & Obst.*, 1938, 66: 962.

2. ASCHOFF, L.: Appendicitis: its etiology and pathology, Constable, London, 1932.

under 14 years of age in which the incidence could be directly traced to acute upper respiratory infection, and in the acute fulminating cases to a preceding gastro-enteritis.

Another hypothesis is that of Ricker,⁷ who puts neurovascular peristasis, prestasis and stasis as the primary functional and anatomical events in appendicitis (Oertel).

The investigations of Wells⁸ are clarifying.

7. RICKER, G.: *Der Stand der Lehre von der Epityphlitis*, 1927, 202: 125.

8. WELLS, A. Q.: *Experimental lesions of rabbits' appendix*, *Brit. J. Surg.*, 1937, 24: 766.

He finds that in rabbits acute appendicitis occurs whenever there is obstruction and a break in the mucosal barrier, the bacteria responsible being those normally present in the lumen.

Summing up, the evidence available at the moment suggests that, while a few cases of appendicitis are of hæmatogenous origin, the majority are enterogenous. The infecting agents are the bacteria normally present in the lumen. The precipitating factor is obstruction caused by a kink or fæcolith. There must be also a solution of continuity of the mucosa. A.G.N.

THE REGULATION OF BLOOD TRANSFUSION

THE use of blood transfusion has become so general that a recent survey by Levine and Katzin of the conditions under which it is practised on this continent is most welcome.¹ This survey was carried out by means of a questionnaire sent to the leading American and Canadian hospitals, and whilst answers were received only from about half of these the information gained is impressive, and in some instances startling.

Some of the points brought out are as follows: (a) The blood group classification most widely used is that with the Moss numbering (IV, III, II, I). The International classification (O, A, B, and AB) is being used more and more, but most of the hospitals still have an arbitrary nomenclature. A plea is made for the advantages of the International method since it so clearly indicates the rationale of the grouping. It is suggested that the schools teach this method uniformly and also that the blood donor agencies make a point of using it. At present most of the hospitals affiliated with schools do not use it.

(b) The methods of giving transfusions vary widely. Less than half of the hospitals use one method only; the majority follow two methods. In 36 there are three different procedures, and in 4 all of the 4 recognized methods are used. The citrate method is the most popular, apparently because it is thought that no special precautions are needed for it. In the New York and New

Jersey hospitals the Lindeman multiple syringe method is the most widely used, but some other hospitals use several varieties of instruments. Slightly less than half of the hospitals use two methods, the citrate and one of the syringe-valve procedures. There is something to be said for this choice of methods.

(c) The important question was asked: Who performs the transfusions? The answer was that in the majority of hospitals the residents and interns do, under supervision either of senior residents or attending physicians. Only in a small group of hospitals, notably in New York City, is there a transfusion team in charge. In more than one-third of the hospitals transfusions are not in the hands of any one department but are done by any one of the attending staff. In several instances the ever-changing house staff performs them with no supervision whatever.

(d) Donors for indigents. Blood is supplied to indigents in a little more than half of the answering hospitals. In 85 hospitals there is no provision for this free supply, and in 43 other institutions it is offered only occasionally, or in cases of most urgent need.

(e) Repetition of Wassermann, Kahn, or Kline tests on donors. Nearly half of the hospitals failed to answer the question on this point. Ninety reported that such tests are performed on donors at intervals of from one to three months. In 112 the interval is six months or more. More significant are the data regarding tests for syphilis just before

1. Blood transfusion in America, *J. Am. M. Ass.*, 1938, 110: 1243.

transfusion. In only 178 out of 350 hospitals is this *always* done; in 36 it is done "frequently or usually"; in 26, only on volunteer donors; in 5, only on professionals; in 83 it is not done.

Other details of interest are brought out, such, for example, as the selection of donors. The importance of this might seem to need no comment, but the number of accidents reported suggests negligence in the technique of grouping. The advantage is strongly emphasized of special transfusion teams in each hospital who shall instruct the interns in transfusion. Such teams might also serve to link up transfusion work between the hospitals of each city. They could regulate professional donors by proper registration, a much needed arrangement, and also serve as centres for studying problems relating to

transfusion. What can be done by concentrated effort in this matter is shown in a report in the same Journal² of the Blood Transfusion Betterment Association of New York City. This Association reports extraordinary growth in activity, its work having tripled in seven years. It would be well for each large centre to follow its example. We know of one large hospital in Montreal in which an exhaustive study of the whole question of transfusion and intravenous injections has been made, but there seems to be a need for wider coordination. The giving of blood transfusions will inevitably and properly increase very rapidly, and the risks with which it is hedged about must receive more serious consideration.

H.E.M.

2. *Ibid.*, 1938, 110: 1248.

Editorial Comments

Medical Students Form an Organization

The medical students in a number of the eastern medical colleges have formed a national organization to be known as the Canadian Association of Medical Students and Interns. The student bodies now sponsoring this new body are the Medical Society of the University of Toronto, the Æsculapian Society of Queen's University and the Hippocratic Society of the University of Western Ontario. The student societies in the other universities have been invited to participate, but official action has not been taken.

The new C.A.M.S.I. has already embarked upon several activities. One of these is the setting up of a uniform date for the appointment of interns. The present system, or lack of it, is not satisfactory to either the prospective interns or the hospitals, and greater uniformity in date would overcome much of the trouble and uncertainty now experienced.

Another activity under consideration is an educational program concerning tuberculosis among the students and the interns. The annual wastage in both the student and the intern bodies is lamentably high. The officers of the new association feel that much could be done to impress upon all concerned the necessity for greater precautions in personal contacts, in daily habits, in housing, and for more adequate time for relaxation. The guidance of outstanding authorities is being sought in this program. No doubt when the different parties get together

many of the situations complained of will disappear. The policy of *laissez aller* has become somewhat ingrained, but all, we think, will agree that the health of the intern is of great importance both to the hospital, to himself and to his relations.

Membership in this new society is open to all medical students and interns in Canada. To expedite organization, the present officers are zoned in the Toronto area, the Chairman being Paul F. McGoey, the Vice-Chairman, D. Harold Copp, and the Secretary-Treasurer, Wm. K. Kerr.

HARVEY AGNEW

International Academy for Post-graduate Medical Work

On April 23, 1938, an "International Academy for Post-graduate Medical Work" was founded in Budapest with Prof. Dr. Borst, Munich, as its President. Vice-presidents are: Prof. Dr. Aree, Buenos Aires, Prof. Dr. Bastianelli, Rome, Prof. Dr. Olivecrona, Stockholm, Colonel Proctor, London, Prof. Dr. Tiffeneau, Paris. The Permanent Bureau is in Berlin and represented by Dr. Blome, Prof. Dr. Adam and Dr. Pütz. It is the hope of the "International Academy" to create an international basis for post-graduate medical work by means of international courses, international instructors, and students' exchange, exchange-study-trips, information offices, etc. Further particulars may be obtained from Prof. Dr. Adam at the Permanent Bureau, Berlin NW 7, Robert Koch-Platz 7.

Retrospect

EUROPEAN TRENDS IN IRRADIATION THERAPY*

BY EVELYN TRAPP, B.A., M.D., C.M.

Vancouver

My tour of Germany began with Berlin and the Charité, largely because of Chaoul and his new low voltage "contact therapy". The most spectacular part of Chaoul's own work was his treatment of lesions after surgical exposure, notably cancer of the rectum. During the time I spent at his clinic I saw one patient who had comparatively recently completed his treatment; his artificial anus had been closed and he maintained that he had returned to a completely normal existence, suffering no inconvenience of any kind. Another was nearing the end of his treatment and seemed to be carrying on without any great suffering. Nine had been treated altogether; 2 showed no favourable results; 6 were cured, the observation period varying from six months to two years. For other lesions treated Chaoul claimed a 93 per cent primary healing for skin cancers, 83 per cent for lips, and 40 per cent for cancer of the oral cavity.

Before leaving the so-called contact-therapy I should like to mention the Schaffer-Witte method for the treatment of cervix cancer. I watched this being carried out by Dr. Witte at the gynaecological clinic of Professor Martius in Göttingen. In addition to the usual intracavity radium and deep x-ray a series of treatments was given with a contact tube inserted in the vagina against the parametrium. This method had been in use for about two years, and Dr. Witte was convinced that primary results were definitely improved.

At the Charité also, in Professor Wagner's clinic, is one of the few supervoltage equipments on the Continent. This had been in use since 1930, first with 400 and later with 600 kilovolts. On the whole, German radiologists do not seem to feel that better results can be obtained than with 200 kilovolts. Holthusen, Holdfelder and Voltz all hold this opinion, which is shared in other countries by such men as Forsell, of Stockholm, Shintz, of Zurich, and Webster, of London.

Holthusen is perhaps the most outstanding of the German radiologists; at least he is the best known abroad. He speaks excellent English and has the advantage of being a physicist of note. Years ago he put the measurement of depth dosage on a scientific basis, and at present and in common with many other research

workers is trying to create a firm basis for general irradiation pathology. This will give a standard for comparing the different methods of irradiation therapy, contact and telecurie therapy, high intensity and protracted and fractional doses, ultra-hard and ultra-soft waves, and will be of inestimable value to radiotherapeutics. The exact knowledge of tumour radio-sensitivity is dependent on the exact knowledge of dosage delivered to a large number of tumours correlated with their histology, and the acquisition of this fundamental knowledge only became possible with the acceptance of the physical in preference to the biological unit of dosage. The unit generally accepted in Europe is the Sievert unit dose (*i.e.*, the quantity of gamma irradiation received in one hour at a distance of 1 cm. from a "point source" containing 1 mg. of radium element surrounded by 0.5 mm. of platinum), which is equivalent under specified conditions to approximately 8 roentgens, and is considered to be sufficiently accurate for medical purposes.

Holdfelder, at Frankfurt, is still working with his six 200 KV "cannons" installed some twelve years ago. He long ago evolved ingenious methods of tumour localization, and his "compression" and tangential treatment of breast cancers have become bywords in the radiological world. He treats many lesions beside cancer — asthma, thyrotoxicosis, tonsillitis, arthritis, post-operative pneumonias, and many of the chronic inflammatory conditions. Believing that he has already learned what can be accomplished with the more easily curable cancers, such as cancers of the lip, buccal mucosa, breast, uterus and tongue, he has now turned his attention to the more difficult types such as bronchogenic cancer and cancer of the intestine, and, like Holthusen, is approaching the problem from the point of view of pathology and physics. Work of this sort is continually adding to the scope and usefulness of radiotherapy. Holdfelder's own clinic is an example of almost superhuman efficiency and order: he says, because run on Nazi principles.

Wintz, at Erlangen, in spite of the opposite trend elsewhere, still maintains the virtue of his "one time" technique. Breast cancers he treats as follows; a single massive dose of irradiation over each of three fields, including the entire "field of extension" of mammary cancer, from the ear to the costal margin, and from the sternum to the border of the latissimus dorsi. Eight days later the tumour is removed by diathermy and examined microscopically. If malignant the ovaries are irradiated to stop the menstrual cycle. The second irradiation follows eight to ten weeks after the first, and this concludes the treatment. Wintz reports a five-year

* A paper read before the Joint Meeting of the British Columbia and Alberta Divisions of the Canadian Association of Radiologists, February, 1938, at Victoria.

cure rate of 50 per cent in operable and 14 per cent in inoperable cases.

Irradiation of the ovaries is based on the theory that the pre-lactation changes in the breast at each menstrual period stimulate any malignancy in the breast. Wintz has practised this as a routine for many years, but its expediency was not generally accepted until recent experimental work, notably that of Lacassagne in Paris, demonstrated that oestrin produces hyperplasia of the acini of the breast, and corpus luteum causes exclusively duct hyperplasia.

Vienna has always been essentially a surgical centre, and still is. It is the only prominent place in Europe where early cervix cancer is still considered a surgical rather than a radiological problem. However, radiological treatment has not been neglected, and since my last visit a large new institute had been established and was carrying on all the most recent forms of x-ray and radium treatment, including telecurietherapy.

New institutes have also recently been opened at Brunn in Czechoslovakia and at Budapest, and these, fortunately, were in easy reach of Vienna. In addition to these, though some time later, I visited a new one in Rome and another in Leningrad; all are large and well equipped institutes, self-sufficient in staff and services, some more luxurious than others, that in Rome being the most spectacular in this respect. But Italy is the home of white marble, and Mussolini likes his buildings on the grand scale. The Masaryk Institute in Brunn was the most impressive from the point of view of the simplicity of its design, yet no other seemed quite so completely equipped or so well coordinated in its various departments. It was completed some four or five years ago, and is unique in that it has been self-supporting from its first year. The largest of the new institutes was in Leningrad. It was carrying on extensive biological research as well as the usual clinical activities. In the treatment of gastric ulcer they claimed consistently good results, as shown by x-ray, the rationale of the treatment being the effect of the rays on the vegetative nervous system. Anna Jugenberg told us they had treated some 900 cases in this way. X-radiation was administered first locally over an area which included stomach, duodenum and coeliac ganglion. One ventral and one dorsal field of 10 by 15 cm. from a distance of 30 cm. were used, doses of 225 to 250 r being given at intervals of 4 to 6 days, twice over each area. Following this a spinal field from the 5th to 12th thoracic vertebra received 250 r twice in 6 days. The series was usually repeated after 5 to 6 months.

All Europe has satisfied itself on the paramount importance of centralization for the successful handling of the whole cancer problem, and more and more institutes are being planned and installed in the different countries.

In Stockholm, as elsewhere, physical measurement of dosage has replaced the original empirical methods, but it is interesting to note that the actual treatments have changed very little. A high intensity technique, i.e., 10 mg. needles for 3.5 to 5 hours, is still used for interstitial work.

The Stockholm method for the treatment of cervix cancer was evolved by Forsell in 1912. Since then over 3,000 patients have been treated. The only changes in that time have been an increase in the quantity and filtration of the radium, the addition of deep roentgen therapy, and, quite recently, that of telecurietherapy. Their results compare favourably with all others, and their methods are used widely throughout the world, notably at the Marie Curie Hospital in London, whose five-year survival rate for the treatment of cervix cancer has not been equalled elsewhere, Stockholm not excepted.

Heyman has recently changed his plan of treatment for cancer of the uterine body. Instead of the original method of placing a single applicator into the cavity of the uterus it is now packed full with a large number of cylindrical applicators of suitable size, the quantity of radium varying from 80 to 200 mg. el. The treatment is done at two sittings with a three weeks' interval and a total uterine dose of from 2,600 to 4,000 mg. el. hours, 10 tubes for 20 hours being the average single dose. A vaginal dose about 2,000 mg. el. hours is also given at one sitting. This was formerly combined with deep roentgen-therapy. Now bomb irradiation is used in preference, Heyman believes with definitely improved results, though five-year figures are not yet available. He thinks telecurietherapy to be particularly valuable with isolated glandular metastases, especially from the ovary and fundus, or with parametrial involvement, or with spread down the vagina to the vulva.

Coming to Paris and the Foundation Curie, the Regaud methods of radium therapy are too well known and too widely used throughout the world to require much comment. The development of the last few years is telecurietherapy. The biggest unit now in use is an eight gram bomb, but with the falling price of radium they are looking forward to the possibilities of larger quantities.

This is also the home of the so-called "Coutard technique", which has been accepted and used throughout the world as the greatest modern advance in deep x-ray therapy. It was interesting to learn that originally the limitations of his equipment forced this method on Coutard, and that his acute and patient clinical observation made its advantages apparent to him. He is still using the same equipment with which he began his work over twenty years ago, not from choice but from necessity. When I was there a year ago he was looking forward to the day when the Foundation could afford to install a

400 KV machine. In the meantime he has joined Max Cutler's new clinic in Chicago.

I might say that I approached the Curie Foundation with trepidation, having been told that one would politely but firmly be shown the door unless prepared to remain for at least six months. My initial appearance was evidently on an auspicious day, for I spent several weeks watching the work and seeing the patients; even the case records were put at my disposal to pore over as I wished.

The meticulous clinical observation of Coutard is one of the most impressive features of this clinic; he himself examined the patients before nearly every treatment. It has brought him to the belief that the radiosensitivity of cancer cells is of a periodic nature, and further that this periodicity is of a rhythmic character and varies with the type of cancer. Working on this theory he is attempting to irradiate cancers during their most sensitive periods and now arranges his treatments in series rather than continuously as heretofore. He believes this to be a particularly valuable procedure in the comparatively radioresistant tumours, for the periods of rest make greater dosage possible. The following are the details of a random larynx case chosen from the records.

	<i>Days</i>	<i>Daily dose</i>	<i>Total dose</i>
1st series	1 to 8	250 to 750 r	3,300 r
2nd "	23 to 26	200 to 250 r x 3	2,600 r
3rd "	43 to 45	200 r x 3	1,800 r
		Total dose	7,700 r
	Left side (lesion)	4,725 r	
	Right side	2,973 r	

The largest doses are given at the beginning of the series. The total dose for larynx or pharynx cases is never more than 8,000 r. Tonsils are given up to 9,000 r.

Coutard has come also to very definite conclusions on pre- and post-operative irradiation of breast cancers. These he summarizes as follows.

1. Some cancers of the breast are extremely radio-sensitive. They have a tendency to early invasion of the lymphatics. They constitute about 15 to 20 per cent of all breast cancers.

2. Others are very highly radioresistant forms with a tendency to metastasize through the blood vessels, generally late.

3. Between these extremes there are about 60 per cent of breast cancers of medium radiosensitivity.

4. The first type presents bad operative conditions and is favourably influenced by radiation. The second type belongs to the domain of surgery, if operable.

5. Radiation preceding operation will reduce the chances of dissemination by surgery for the first type; post-operative radiation in the second type may maintain the cure by the destruction of the cells which have become temporarily radiosensitive following surgical intervention.

6. In highly radiosensitive tumours a daily dose of 200 r during 40 to 60 days up to a total dose of 8,000 r

is adequate. In radioresistant cancers the higher daily dose of 400 r to 500 r applied in a series of 2,500 to 3,000 r in 6 days, in 2 to 3 series, with the same total dose of 8,000 r seems sufficient.

Whether one agrees with all Coutard's conclusions or not, one must respect opinions that have been formed on the basis of 20 years of painstaking clinical observation and control.

On my last visit Brussels clinics were the only ones which had attempted anything beyond purely empirical methods of radium treatment. These had been learned through the trial and error of individual experience, and dosage had been expressed in milligram element hours or millieuries destroyed. Murdoch and Simon, in collaboration with Stahel of the university physics department, evolved a method of measuring the dose received by the tissues instead of the dose emitted by the radiant source, i.e., the amount of energy actually absorbed; this was expressed in ergs per cm. Isodose curves were made for the different strength apparatuses, thus enabling the irradiation plan to be first worked out on paper and reducing to a minimum the actual handling of radium. In using these measurements for interstitial work it was found that a tumour of small size could be homogeneously irradiated by putting the needles only into the surrounding healthy tissue instead of into the tumour as heretofore, thus obviating the danger of disseminating cancer cells by direct traumatization. Later the dose was expressed in roentgens instead of in ergs per cm.; similar methods are now used in all the recognized European centres.

In Manchester this method was still further simplified by Ralston Paterson, working in collaboration with Parker, the physicist at the Holt Radium Institute. Sievert's ionization chambers were used for measurement, and methods of homogeneous irradiation were planned first for surface application and single plane implants; later, for two plane implants and for cylindrical applications. Finally, volume implantation was undertaken on this accurate basis. Many hundreds of measurements were made before the "Parker-Paterson" tables were compiled. These have been used routinely by a large staff over a period of years, and have been adopted in many of the other British centres. Very extensive or new types of implants are radio-graphed, reconstructed, and measured by means of the usual Sievert chambers. If there are any points of too low or too high intensity these are eliminated by further implants or the withdrawal of needles, as may be necessary. In this way the same treatments can be carried out by a large and changing staff and in other clinics. This type of carefully thought-out scientific work has made Manchester the most popular teaching centre of Great Britain, and many of the new centres are directed by men trained in the Holt Radium Institute. One important and stimulating feature is the daily "twelve

o'clock clinic" which is attended by the whole staff; here all new patients and all recurrent cases are seen and their treatment prescribed. In addition to this there is a weekly staff conference, when individual treatments are brought up for discussion and criticism. Relevant pathology is discussed, as are also different types of treatment as reported in the current literature. It is an inspiring clinic to visit and to work in. It was my good fortune to fall into a vacancy on the staff, and from a practical point of view these months were the most profitable period of my two years' tour.

Dr. Paterson believes that the spacing of dosage is the important thing and not the actual intensity. He has deliberately set out to prove this contention by treating with intensities in the neighbourhood of 100 roentgens per minute. Thus the time of the daily treatment is very short, 2 to 4 minutes, but the overall-time of a series is analogous to that employed by Coutard, the total dose varying with the total time of treatment. For instance a tumour dose may range from 5,000 to 6,000 roentgens over a period of from 5 to 6 weeks, to 10,000 roentgens in 10 weeks. Much smaller doses are given when the treatment is deliberately only palliative; 2,000 roentgens in four days to 3,000 in 10 days.

The most interesting and best controlled piece of research in London is that of beam therapy under Constance Wood. This is being carried on with three five-gram bombs, two at the Radium Institute, and one at the Royal Cancer Hospital, and its object is the development of a scientific system of treatment that can be repeated in any radium centre. With this idea in view the type of case treated is limited to carcinoma of the pharynx, larynx and upper air passages. Accurate direction of the beam and its measurement in roentgens received in the tissues have been achieved by means of a directional calliper and calculator. This information is graphically recorded, showing the number of roentgens received daily by the tumour, glands and skin. At the same time a graphic record is made showing the response of the tumour, glands, mucous membrane and skin to the dose delivered. Their first five-year period is nearing completion, and valuable and reliable information will shortly be forthcoming.

Telecurietherapy in Europe holds a somewhat analogous position to the supervoltages of America. At least the same hope is expressed for the possibilities of its future development, depending of course on the availability of radium. At the present rate of its production it will soon be a drug on the market if it cannot be used in mass quantities. In this last year the Canadian Eldorado Gold Co. has lent the National Radium Trust of Great Britain 20 grams at the charge of 5 per cent per annum of the current market price. At present, bombs up to 8 grams have been in operation for some years, and the telecurie department of the new

Radiumhemmet in Stockholm is so constructed that quantities up to 100 grams can be safely used. Sievert, their physicist says "There are no technical difficulties in designing suitable equipments for teleradium treatment, even with very large quantities of radium (50 to 100 g.)"

Stockholm is perhaps the most enthusiastic exponent of beam therapy. Berven believes that he has obtained results in his mouth cases which would not have been possible by any other means. One does not hear the talk of supervoltages that is so common in America. The great majority of European therapists feel that equally good results can be obtained with voltages of 200,000. A few equipments with voltages of from 400,000 to 600,000 have been installed, notably in Germany and in Italy, but no great enthusiasm was manifested over the superiority of the results obtained. A million volt equipment was installed at St. Bartholomew's in London in 1936. When I was there experiments in physical measurements were still being carried out. During the last few months patients have been treated with the tube operating at a voltage of 700,000 and a current of 5 milliamperes. No reports are yet available.

As between the two methods, Lacassagne sums up the position very well when he says "From the therapeutic point of view radium could completely replace x-ray in the radiotherapy of cancer. From the same point of view x-rays could take a place exclusively in telecurietherapy. Practically, even when we take into consideration the services which the new apparatus of roentgentherapy at a short distance (contact therapy) may render, the small curietherapy foci in the form of tubes, moulage, needles, etc., made for superficial, intracavitary or interstitial applications, seem destined to endure as long as the radiotherapy of cancer itself."

It may be of interest to note some methods of treatment used but not generally adopted.

1. *Irradiation of the pituitary* to retard its effect on growth. This has been carried out on a large scale by Voltz, of Munich. He has reported 1,936 cases, but the results are still not definite as regards its value.

2. *The association of x-ray with other physical or chemical agents.*—For years attempts have been made to increase radio-sensitivity by such means, and a great variety of organic compounds and many of the elements have been tried. Maisin, of Louvain, is a recent exponent of this possibility, and with minute doses of saccharide of barium has reported the disappearance of small superficial tumours; and by combining this agent with Coutard's x-ray method he appears to be improving on Coutard's results in cancer of the hypopharynx.

3. *Ultra short wireless waves* in combination with deep x-ray therapy.—Two years' research work on this method has recently been completed in Newcastle with very promising results.

4. *General physiotherapy*, such as quartz light, diathermy, irrigations, and baths of various kinds, used solely to improve the general physical condition of the patient. The institute at Brünn has its whole basement fitted up for treatments of this kind.

5. *Teleroentgentherapy*.—For cancer this is based on the theory suggested by clinical and experimental facts that if there is any resistance against cancer it may result from the activities of the reticulo-endothelial system, and attempts have been made to stimulate this system with small doses of x-ray, either by local treatments or by teleroentgentherapy. This was used some twelve years ago both in the United States and in Europe, but the method was largely dropped and has only lately been revived and is now quite widely used in the leukæmias and in advanced Hodgkin's disease.

Mallet, of Paris, has recently treated 290 cases and reported at the International Cancer Congress at Brussels a number of successes in apparently hopeless metastatic cancer. In bone metastases, teleroentgentherapy is found practically always to recalcify the bones and diminish pain. In lung metastases and in œsophageal cancer remarkable results were claimed. He also reported regression in metastases of breast cancer and in advanced cancer of the uterus. By his method teleroentgentherapy entailed no modification in the irradiated viscera. Neither epilation nor erythema was observed, the danger lying solely in the action on the blood. Weekly blood examinations were carried out and when the white blood cells dropped below 2,500 and the red cells below 2,600,000, a rest of three or four weeks was instituted. The treatments were spread over periods of from two to six weeks with four to five irradiations weekly. His technique comprised irradiation of very broad segments, or of the whole body. The anticathode skin distance was from 1.20 to 3 metres; kilovoltage 180 to 300; filtration $\frac{1}{2}$ to 1 copper; a single dose from 25 to 50 roentgens; the total dose from 500 to 1,200 roentgens per field and per series. This radiologist is of the opinion that the mechanism of the action of radiations is different from that of ordinary localized treatments, and presumes that the modifications in the tissue in which the neoplastic cell develops participate in the disappearance of this cell, the seat of the cancerous cell being rendered unfit for its growth. Previous irradiation and infection play an impeding part in this as in other forms of irradiationtherapy.

Briefly, the high lights of development for this period from 1931 are:

In x-ray therapy.—Protraction and fractionization of x-ray dosage, first initiated by Coutard. Low-voltage contact therapy of Chaoul. The widespread use of isodose charts for the measurement of tumour dosage, and the acceptance of the roentgen as the unit of measurement. The increasing use of x-ray therapy in chronic in-

flammatory conditions. The re-awakening of interest in teleroentgentherapy. The growing tendency to separate the work of the radio-diagnostician from that of the radio-therapist.

In radium therapy.—The rapidly increasing use of large quantities of radium, i.e., telecurietherapy. A trend toward surface in preference to interstitial radium treatments, because of the necessary tissue traumatization of the latter type.

A trend away from the clinical use of radon; few new plants are being installed. Manchester still uses the output of its original emanation plant. Paris and Brussels have confined its use largely to animal experimentation; the reasons given being: traumatization of tissues, as with interstitial element needles, and the fact that a foreign body must often be left permanently in the tissues. Also the initial high intensity with the rapid falling off of dosage is thought by many to be a disadvantage.

The replacement of the first empirical methods of radium dosage by accurate physical measurements by means of ionization chambers. This has made it possible to measure the dose received by the tumour rather than that given by the source of irradiation; and to arrange the tubes so that a uniform dose can be given. This together with the widespread acceptance of the roentgen as the unit of radium as well as of x-ray dosage has put the measurement of both these therapeutic agents on a truly scientific basis.

In general.—Improved methods of tumour localization by means of radiography and clinical measurements and variously designed charts, such as Holdfelder's atlas of cross-sections of the trunk.

The attack on the problem of intractable pain. In Great Britain, research grants are provided specifically for this purpose. Rowbotham and Todd, of Manchester, have been able to demonstrate some very gratifying results with alcohol injection of nerve ganglia and resection of nerve trunks, in both mouth and pelvic cases. This goes hand in hand with the increasing tendency to treat the patient as well as the disease, particular attention being paid to the blood picture and to the diet. In earlier days the tendency was to concentrate on the cancer alone and its reaction to treatment.

The establishment of clinical research on a solid foundation.

Increased cooperation between surgeons and radiologists, a direct result of centralization. Efforts made to comply with the international recommendations for the protection of x-ray and radium workers.

Centralization for therapy by the establishment of self-contained units, either as a part of a general hospital or, when finances permit and population justifies, a separate institute. This latter is universally considered to be the ideal. These institutes have complete facilities

for the diagnosis and treatment of cancer, including surgical as well as radiological treatment. They have, in addition to the usual ancillary services of a hospital, their own pathological and physics departments, and provision for research work. This of course varies greatly from one institute to another; some are limited to clinical research alone. All have follow-up systems and make a point of accurate statistical records.

Irradiation therapy is in an inspiring stage of development; its early beginnings date back nearly forty years; enough time has elapsed to judge the factors of enduring value; the useless has been discarded. We know definitely that a large percentage of early cancers can be cured if treated adequately, and we know from experience what adequate treatment is. There are still certain groups we cannot touch, but if progress continues, as it undoubtedly will, these problems must also be solved.

There are of course divergences of opinion on methods of treatment; the intensity argument still continues for both x-ray and radium. For example, Regaud, of Paris, and Murdoch, of Brussels, both believe that the intensity of interstitial and surface radium treatments should be low, the treatment period extending over a period of days; while Berven, of Stockholm,

maintains that high-intensity treatment lasting for a few hours is equally efficacious and much more practical. All have excellent results to show. One must therefore conclude that the important matter is to treat the lesion with the optimum dose for the time of irradiation and for the type of cancer under consideration. For extensive lesions one has the impression that low intensity is the method of choice.

Supervoltages and telecurietherapy seem to be the research problems of the future. America, with her great financial resources, has taken to herself the supervoltage problem. Centres in other countries have visualized the possibilities of treatment with radium in vast quantities, even from 50 to 100 grams, but up to the present radium has been too scarce and too costly for this interesting research problem in telecurietherapy to be undertaken. Canada is now taking first place in the production of radium. The ores in the Great Bear Lake region are the richest so far discovered in the world, and their supply is apparently inexhaustible. This fact foreshadows enormous reserves of radium. It would therefore seem natural, and highly desirable, for Canada to take advantage of her good fortune and demonstrate to the world the effect of radium *en masse* in the treatment of cancer.

Special Articles

DIET AND NUTRITION

NUTRITIONAL REQUIREMENTS OF THE MOTHER DURING LACTATION*

By I. M. RABINOWITCH

Montreal

V.

Premature births and still-births are common amongst undernourished women. When fetuses of such women do reach maturity and are born alive they are usually underweight and many die within the first ten days of life. Amongst those which survive for longer periods of time, the chances of living long, unless they are artificially fed, are greatly reduced because of the diminished capacity of the undernourished mother to produce milk. Food is, of course, not the only factor which governs the physical fitness and survival of the new-born infant; heredity plays its part—the capacity to grow is inherent in protoplasm independent of food supply. However, as Todd¹ aptly put it, the

adult physical pattern is the outcome of growth, along lines determined by heredity but enhanced, dwarfed, warped or mutilated in its expression by the influence of environment in the adventures of life. One of these influences is food supply.

The possible effects of diminished capacity to produce milk upon the nutrition of the infant are suggested from the relationship between the protein contents of milk of different species and the average time it takes for these species to double their birth weights.² Thus:

Species	Protein content of milk percentage	Number of days required to double birth weight
Human	1.6	180
Horse	2.0	60
Calf	3.5	47
Kid	4.3	19
Pig	5.9	18
Lamb	6.5	10
Dog	7.1	8
Cat	9.5	7
Rabbit	14.4	6

The metabolism of lactation is not entirely a post-natal phenomenon; the preparation for this function begins practically with the onset of

* This is the fifth in the series of articles on Diet and Nutrition, prepared under the auspices of the Association's Committee on Nutrition. The previous articles can be found in the *Journal*, 1938, 38: 277, 387, 491 and 586.

pregnancy but, as will be seen later, is much more active during the latter months. Some idea of the necessary preparation is suggested from a comparison of the chemical composition of the mother with the chemical composition of her new-born infant. A full term infant, weighing about 8 pounds, contains about 60 grams of nitrogen only; yet, by the time the pregnancy has reached full term the body of a pregnant woman acquires about 500 grams of nitrogen in excess of that present prior to the occurrence of the pregnancy, that is, about 800 per cent more than that which can be accounted for by the nitrogen content of the fetus. In the case of calcium the excess is about 50 per cent, and that of phosphorus is 300 to 400 per cent more than can be accounted for by the fetus.³ The increase of weight alone suggests an appreciable storage of food materials.* Some of this excess can be accounted for by the amniotic fluid and the placenta. An appreciable portion is to be found in the increase of the uterine musculature. A part is necessary to counterbalance the marked loss which occurs immediately after birth and here we observe a somewhat similar behaviour of mother and infant. Prior to its birth the infant stores an excess of iron because of the marked destruction of blood which occurs within the first ten days or two weeks of life. Because of the poor calcium content of human milk the infant also stores large amounts of this element prior to its birth. The mother stores food materials for somewhat similar reasons. Nitrogen is an example. The retention of this element is particularly marked during the last few weeks of pregnancy, ranging from 1.4 grams a day in primiparae to over 5 grams a day in multiparae.⁴ The storage counterbalances to a very appreciable extent the loss of nitrogen which takes place immediately after the birth of the child and which continues until about the end of the third week on account of the regressive changes. This daily loss of nitrogen may amount to as much as 4 grams or more.⁵ All of these factors, however, do not account entirely for the storage of nutrient materials in the maternal organism during pregnancy. An appreciable part is to be found in the enlargement of the breasts in their preparation for the production of milk.

A fact of practical importance is that nutritional disturbances which occur as a result of inadequate storage of food in the maternal organism during the intra-uterine life of the child are very difficult to counteract after birth, in spite of very careful feeding. For example, a child whose mother suffered from osteomalacia during the pregnancy is likely to develop rickets,

regardless of the satisfactory diet of the mother during lactation and use of supplementary diet for the child which contains all of the essential food elements.

The above examples were cited to emphasize the fact that a consideration of the nutritional requirements during lactation is incomplete without consideration also of the requirements during the preparation for lactation and the development of the fetus. Yet, according to the Children's Bureau, the nine months before a baby is born are "the most neglected period of its existence".⁶

Assuming conditions are normal for both mother and child at the end of the period of gestation, deficiencies may still occur and thus not only affect the nutrition of the mother but indirectly also that of the child. A guinea pig runs about and nibbles green leaves soon after it is born. Like other mammals, however, the new-born human infant is helpless and must obtain its entire food supply from its mother. It does not have to be taught the principles of hydrostatics to do so; but knowing how to feed and obtaining the proper nutrient materials, qualitatively and quantitatively, are not synonymous.

The nutritional requirements of a woman during lactation have materially changed in the last few centuries. In the 16th century, a mother did not wean her child until it had all of its teeth. This, as the writer has observed, is still a practice amongst some Eskimos in Canada's Eastern Arctic. Today, amongst civilized peoples, the child is generally weaned before it is one year old. This practice is compatible with the health of the child, because of the advances made in the science of infant feeding. Human milk is, however, not as yet entirely reproducible. It is, therefore, necessary to know the conditions under which the child may receive an adequate supply of milk without impairing the health of the mother.

The production of milk does not, *per se*, demand a great expenditure of energy. The rearrangement of food of the maternal organism for the preparation of milk depends upon hydrolytic changes (cleavage and synthesis) which involve hardly any thermal reactions. The secretion of the milk, like secretion by the kidneys, has also little influence upon the total energy exchange of the body. The additional food necessary for the maternal organism for the production and secretion of milk is therefore negligible. The chief consideration during lactation is, as will be noted, the loss of the food materials in the milk and storage of a certain amount of food which cannot be accounted for entirely by the chemical composition of the milk.

Human milk contains about 1.5 per cent of protein, 3.5 per cent of fat, and about 7.0 per cent of carbohydrates. One litre of such milk,

* By full term, a woman weighs about 30 pounds more than before the pregnancy. The child accounts for 7 or 8 pounds. The placenta, etc., account for another 7 or 8 pounds. During pregnancy, therefore, the maternal organism, *per se*, acquires about 15 pounds of weight.

therefore, has a food value of over 600 calories and a litre of milk is, approximately, the daily requirement of the child during the latter months of breast-feeding. Milk production can be forced in animals and man is no exception. Amounts as high as 1,521 and 1,758 cubic centimetres have been observed with energy values of 1,269 and 1,096 calories respectively.⁷ A fact of practical importance in these observations is that production of milk can be forced by a proper food supply. Equally important, however, is also the fact that the drain upon the maternal organism may be quite appreciable. For example, since human milk contains about 0.03 per cent of calcium, these subjects lost between 0.45 and 0.52 grams of calcium per day. Human milk, it was noted, contains about 1.5 per cent protein. The protein losses in these cases were, therefore, about 25 grams a day.

As a guide to the nutritional requirements of the mother during lactation, the following are, briefly, the more important facts.

1. Milk is a true secretion; it is the product of the cellular structure of alveoli of the mammary gland. As stated, its production requires little energy and, like the kidney, its secretion does not involve an appreciable expenditure of energy. However, the food requirements of the mother are not to be judged entirely by the food value of the milk; proper production of milk is accomplished only by simultaneous storage of similar food materials in the maternal organism. Without such storage either the amount of milk is reduced or the mother loses weight.

2. The food requirements are not uniform during the entire period of lactation. When one week old a child may consume about 15 ounces of milk during 24 hours; whereas three weeks later it may consume twice this amount. Milk production tends to reach its peak between the 25th and 30th week. This is shown in the weekly consumption of calcium by the nursing infant (Rose*). Thus:

<i>Age of infant (months)</i>	<i>Weekly consumption of calcium (grams)</i>
3	1.9 to 2.2
6	2.5 to 2.7
9	2.7 to 3.0

Failure to recognize these changes in milk production and, therefore, the changes in the nutritional requirements of the mother may account to quite an extent for losses of weight of the maternal organism at these periods.

3. The caloric needs of the mother are met with by allowing, in addition to the mother's own needs, approximately 60 calories per day for each pound of the infant's body weight

* The calcium content of human milk ranges within very narrow limits. The total grams of calcium, therefore, afford a reliable indication of the volume of milk consumed.

during the first three months; about 50 calories during the second three months and about 40 during the third. These are liberal values, since very few children are now entirely breast-fed. A number of means of conserving calories were outlined briefly in the first of this series of articles.⁸

4. An adequate supply of protein is assured by supplying about 2 calories in the form of protein for each protein calorie present in the milk. The protein should, however, have the highest possible biological (protein-sparing) value and, therefore, should be in the form of milk, eggs, fish and meat. Although liberal servings of bread and other cereals are desirable as sources of energy, no reliance should be placed upon these food materials as sources of protein because of their relatively low biological value.

5. A deficiency of calcium during lactation is more likely to occur than of any other of the food elements.* A minimum of one quart of milk a day, supplemented by an average portion of cheese once or twice a week, combined with eggs and green vegetables will, however, ensure an adequate calcium intake. Cod liver oil is an additional safeguard since it enhances the utilization of calcium (and phosphorus).

6. It appears that the bovine organism may be capable of synthesizing vitamin C. There is, however, no evidence that the human being can do so. A liberal serving of fresh citrus fruits twice a day or, if necessary, canned tomatoes protects against this deficiency. The modern methods of canning do not destroy this vitamin.

7. A liberal serving of vegetables twice a day is desirable. Half of it should be raw.

8. With the above liberal amounts of milk, meat, eggs, fruits and vegetables, no special precautions are necessary to meet the requirements with respect to all of the other vitamins. The total mineral requirements will also be met satisfactorily.

9. The total daily intake of fluids should be no less than two quarts; more is desirable. Such amounts tend to increase the volume of milk. As stated, although the chemical composition of milk differs in different species it is fixed within narrow limits in each species. No increase of calcium in the diet, for example, can appreciably increase the percentage of calcium in the milk. Since human milk is poor in calcium an adequate supply for the child is, therefore, obtainable only by increasing the volume of the milk.

10. Lactating women tend to become anæmic, not only because of a deficiency of iron in the diet but because of impairment of the mechanism of utilization of this mineral due to the

* This was strikingly shown in dairy cows; when bred to a high producing capacity (20 to 27 pounds per day) calcium equilibrium could not be maintained by diet and adequate sunlight alone; additional quantities of anti-rachitic vitamins were required (Hart, E. B., *et al.*: *J. Biol. Chem.*, 1926, 67: 371).

tendency towards defective production of gastric secretion during pregnancy. Large amounts of iron tend to counteract this tendency and are assured by the above-mentioned liberal use of eggs, green vegetables, etc. A fact also of practical importance is that prevention of iron deficiency is dependent not only upon the amount of iron in the food but also upon the form in which the iron is supplied. Judging from the rate at which hæmoglobin is produced, the combination of bread and eggs or bread and meat—particularly liver and chicken gizzard—appear to be the most satisfactory. Utilization of iron is also influenced to some extent by the calcium content of the diet. An adequate intake of calcium, therefore, serves another purpose.

11. Finally—and it cannot be emphasized too often—a consideration of the nutritional re-

quirements during lactation is incomplete without a consideration also of the nutritional requirements during the period of the preparation for lactation; the proper time to prevent deficiencies is not after the child is born, but soon after the onset of pregnancy.

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Medical Economics

MEDICAL ECONOMICS

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Medical economics has always been of peculiar interest to both the public and the profession. The generosity of the physician which has been so much admired by the public has led to a state of confusion—to the public, in that the service which they get from the profession has always been considered in the form of a necessary evil, falling in most uncertain times and places and out of which developed a relationship making it easy for the former to leave the "Doctor's bill" last to be paid and at the same time making it difficult for the physician to insist on prompt payment, thus frequently leaving him in serious financial embarrassment.

The lack of appreciation in this regard has led in most European countries to the institution of state-controlled medicine, which in most instances was formulated upon straight economics without due consideration of the needs for good service. This has resulted in years of turmoil, dissatisfaction and quarrelling. In Great Britain this period lasted from 1912 to 1926 and has not yet entirely passed. Recent events have demonstrated that the cooperative spirit is more in evidence.

Until recently the profession in Canada has continued this attitude of critical indifference, with unsatisfactory results. It is the profession's duty to be constructive and helpful in matters so vital to their own welfare. If we continue to put the telescope to our blind eye in regard to our own peculiar problems we can most certainly expect that the public will take us by the forelock and force us into considera-

tion of the problem and perhaps, twenty years hence, as they have found in England, we will find that our lot has improved despite our own obstinacy. How much better that lot will be if the profession will do the leading. The architect must know before the house will be what the builder wishes. If the medical men leave the building to others they may well fear state-controlled medicine. If they themselves will evolve "health insurance" they can look forward to a system which will be of equal pride and value as their endeavours along scientific lines.

Realizing these facts, the Ontario Medical Association has given financial and moral support to Associated Medical Services, Incorporated. The fine cooperation of the Toronto Academy of Medicine with the Ontario Civil Service Association has done much to facilitate the establishment and progress of Associated Medical Services.

In arriving at a basis of service and its cost, we have considered it best to set out the services required by an individual in one year* and set over against it the cost on the basis of the minimum schedule of fees as set forth by the tariff of the Ontario Medical Association. This appears as follows:

Home calls—1 per person per year.....	\$3.00 each
Office calls—1.5 per person per year at \$2.00	3.00 "
Surgical operations—0.08 per person per year	
at \$50	4.00 "
Consultations and specialist cost per person	
per year	4.00 "
X-ray and laboratory work.....	1.00 "
Hospitalization—1.3 days at \$3.50.....	4.50 "
Nursing—0.05 days at \$5.00 per day.....	2.50 "
Administration	2.00
Total	\$24.00

* The figures for service are the result of wide study and research over a period of four years and are drawn from sources too numerous to list.

These services cover obstetrical and surgical attention under controlled conditions, and the cost totals \$24.00 per person per year in the individual situation. Because of the reduced incidence of service required in the family situation the cost drops 25c. for each dependent to a minimum of \$1.00 per person. In the average family of four this costs \$6.50 per month, or 5 12/32c. per day per person. This is less than is spent annually by such average family on smokes, cosmetics or other luxuries.

On April 9, 1937, Associated Medical Services secured a non-profit, non-share charter from the Ontario Government. On June 1, 1937, we opened our offices for subscribers in space granted by the Ontario Government at No. 11 Queen's Park, Toronto.

The following table gives a statistical summary of our growth and progress.

obligations to the full but we have accumulated a reserve of 105 per cent of the total cost of those obligations. After all advance payments are deducted we have over \$3,000 left for reserve. It must however be borne in mind that there are certain factors, such as obstetrics, which have not become fully apparent. There are no doubt others that experience will disclose which will alter this ratio to some extent. It is fairly obvious, however, that 105 per cent is ample to care for these.

A start has been made on the evolution of an equitable method of medical economics with a method of control in which the needs of all parties is given due consideration. A good house is never built from the roof down. We must build from the ground up, slowly, surely and steadily. Experience must always take precedence over expediency.

BUSINESS SUMMARY

Date	1 No. of subscribers	2 Increase per month	3 Administration cost rate	4 Monthly income	5 Total reserve collected	6 Medical accounts paid	7 Reserve in bank
1937			percentage				
June 30	85		67	\$ 157			
July 31	147	62	57	276			
Aug. 30	210	63	65	388	\$ 74		\$ 74
Sept. 30	281	71	72	518	185	\$ 12	173
Oct. 31	419	138	58	775	682	100	339
Nov. 30	629	210	44	1,163	1,214	163	1,050
Dec. 31	733	103	41	1,357	2,058	336	1,222*
1938							
Jan. 31	929	196	36	1,700	3,181	782	1,898
Feb. 28	1,119	190	34	2,060	4,431	1,337	2,593
March 31	1,352	243	30	2,500	6,064	2,095	3,469
April 30	1,560	208	30	2,885	7,794	3,100	4,194

Column 6 represents 90 per cent of third and subsequent premiums paid in advance and included in column 5. Advance payments at April 30th were \$800, leaving a net reserve of \$2,300 after allowing for the April accounts which are outstanding.

* During the month of April it was found necessary to utilize \$500 of the free reserve as of December 31, 1937, for administrative expense.

In considering this summary there are two facts which should be borne in mind. First. June, July and August are the holiday season, and therefore difficult months in which to carry on business of any type. This holiday slump is again apparent in December. The second point is in relation to the incidence of illness. During the month of July there is an average of 6.1 per cent of the population under medical care. This rises progressively to 11.5 per cent during the months of January and February. It falls to 9.4 per cent in March and drops progressively to its low of 6.1 per cent again in July. Associated Medical Services has passed through the period of the heaviest incidence of illness in the year. Not only have we met our

From this beginning the profession in Canada can build a system of medical economics which will not only improve their financial lot but will afford us the opportunity of cleaning our dwelling which is generally recognized as being long past due. This is our problem. Let us meet it. Our own inertia and fear are our greatest obstacles.

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Hospital Service Department Notes

Educational Films

Enquiries are made at frequent intervals concerning the availability of educational films in Canada. In an effort to ascertain the extent to which films are available, the Department of Hospital Service of the Canadian Medical Association has made enquiry from various sources, and a summary of the information received may be obtained upon application.

It would appear that some of the voluntary health and other associations in Canada have a number of films available. For instance, such may be obtained from the Canadian Tuberculosis Association, the Health League of Canada, and the Ontario Safety League. Certain commercial organizations in Canada have films on various subjects. These firms include Mead Johnson & Company, of Belleville, the Metropolitan Life Insurance Co., Ottawa; and the Winthrop Chemical Co., of Montreal. The Department of Agriculture at Ottawa has certain films on milk. The Province of British Columbia has a film on venereal disease, and one on tuberculosis. The Saskatchewan Provincial Government has a film on cancer, and the Anti-Tuberculosis League one on sanatorium care. Quebec has a number of films. The Eastman Kodak Company has a number of films that may be purchased, and the Associated Screen News, Ltd., Toronto, has health films for rent. In addition a great many films of United States origin are available. These are issued by the American Society for the Control of Cancer; the Rockefeller Foundation; the American College of Surgeons (35 mm. "Good Hospital Care", with sound, available through the Department of Hospital Service of the Canadian Medical Association); the British Film Institute, 4 Great Russell St., London; American Dental Association; American Social Hygiene Association, and a number of commercial houses, such as, Eli Lilly Company; Belgard & Spero; Libby, McNeill & Libby, and other organizations. Catalogues of films are issued by the American College of Surgeons, and by the Bell & Howell Company, of Chicago. Most of these films are 16 mm. and silent, although some are with sound, and a number are available in 35 mm. size.

The problem of duty, when films are imported from the United States, has not been satisfactorily settled as yet. Item 696a was inserted in the Canadian Tariff, to implement the provisions of an International Convention signed at Geneva by a great many countries of the world, with a view to facilitating the international circulation of films of an educational character. This item provides free entry, when

the films are accompanied by a certificate of the government or an official of the government, recognized for that purpose, of the country in which the film is produced as to its educational character. Unfortunately, so far, the United States, which is the source of a large number of desirable educational films, although a signatory to the International Convention, has not yet set up machinery to certify films to be exported from that country. Until such time as the United States takes this necessary step, American films cannot be imported into Canada free of duty. England and other countries of the British Empire have set up this machinery. Except when permitted under Item 696a, 16 mm. positive moving-picture films come in under Item 463, which is free under the British Preference schedule, 20 per cent under the Most Favoured Nations and Intermediate Schedules, and 25 per cent under the General Schedule and the French Treaty. In addition, there would be the usual excise taxes, and the sales tax unless brought in by a public hospital. It is understood that rebates of the duty may be arranged upon the return of the films. In view of the importation difficulties the use of films which must be imported directly from the United States cannot be recommended until such time as the entry of such films under Item 696a can be arranged.

Medical Societies

Montreal Medico-Chirurgical Society

The annual meeting of this Society was held on May 20th, when the reports of work for the year were presented. The address of the retiring President, Dr. D. S. Lewis, commented on the large attendance at the meetings throughout the year, and particularly on the success of the three day convention held in the fall. The Program Committee plans to make certain innovations for next session's work. Dr. Lewis then turned to the history of the Society and presented many interesting details regarding its development. He had been informed that it was originally a French organization, but the records did not support that statement. The minute books are nearly all intact and provide records of great value. The Society was founded on September 23, 1843, when a group of doctors met at Dr. James Crawford's house at 28 Little St. James Street. Its association with McGill University was then and always has been very close. Of the 41 original members 13 were on the teaching staff of the medical faculty, and the period of unsettlement in medical education in Montreal during the early 'fifties was reflected in the fact that the Society suspended operations for some years at that time. It was revived in 1865 by the efforts of Drs. Hingston

All communications intended for the Department of Hospital Service of the Canadian Medical Association should be addressed to Dr. Harvey Agnew, 134 College Street, Toronto.

and Palmer Howard, and a bilingual Society was formed, the minutes being kept in French and English. But after five months' existence it again lapsed and was started once more in 1870, Drs. Hingston and Howard again being the active figures. Dr. T. A. Roddick was secretary and his minutes were a matter for pride.

Dr. Lewis then turned to that apparently unfruitful aspect of the Society, its finances, and with great skill drew from it extremely interesting and valuable information. He made the significant point that general practitioner's fees, according to the tariffs recorded in the minute books, have not altered to any great extent, whilst the specialists have had "much greater success in educating the public." Then he gave instances of expenditure in the Society which were of more local interest. Expenditures had gone up in recent years because the Society had very greatly developed its activities, but it was still able to lay aside something each year.

It is to be regretted that Dr. Lewis' entire address cannot be given here.* It is of necessity largely concerned with domestic details of the Society, but it is to be commended as an excellent instance of wise comparison with the past, using it as both a guide and an inspiration.

The Montreal Physiological Society

ON THE DISTRIBUTION AND RATE OF DISAPPEARANCE OF INJECTED HISTAMINE IN NORMAL AND ADRENALECTOMIZED RATS.—Bram Rose and J. S. L. Browne. (From the McGill University Clinic, Royal Victoria Hospital; abstract of paper read on March 21, 1938).

Histamine hydrochloride was injected intravenously into adult etherized female rats of the "hooded" strain. At varying time intervals, the animals were again etherized, the blood and tissues removed and their histamine content determined, in the blood by the Code modification of the method of Barsoum and Gaddum, and in the tissues by the method of Best and McHenry. Assays were done on the atropinized guinea-pig ileum, and some of the values for tissues were checked using the blood pressure method in the atropinized cat under ether.

A dose of 0.04 mg. histamine hydrochloride per gram of body weight was chosen since this was in general well tolerated by the adrenalectomized group which was maintained on 0.9 per cent NaCl.

In both normal and adrenalectomized animals the histamine disappears at a very rapid rate from the blood, even at the end of 15 minutes the distribution is markedly in favour of the tissues. Of the tissues studied the kidney shows the highest concentration. At the end of fifteen minutes only a small fraction of the

histamine injected can be recovered in the tissues studied. In the normal animals the rate of disappearance of histamine is greatest in the kidney; and the concentration has fallen to normal levels in lung, liver and glands at the end of two hours. After adrenalectomy the rate of disappearance from both blood and tissues is very much slower. The mechanism of destruction of histamine seems to be impaired after adrenalectomy.

DIABETIC COMA.—I. M. Rabinowitch. (Abstract of paper read on March 21, 1938).

By making use of the combined physiological properties of unmodified insulin and protamine zinc insulin it was shown that protamine zinc insulin is not only not contraindicated in the treatment of diabetic coma, but is the ideal method of treatment. With one simultaneous injection of unmodified insulin intravenously, unmodified insulin subcutaneously and protamine zinc insulin subcutaneously, the dose depending upon the severity of the coma, the blood sugars are rapidly reduced to the normal level, glycosuria and ketonuria disappear, and the blood sugar is kept normal from 24 to 60 or more hours, in spite of hourly administration of carbohydrates ranging between 300 and 1000 or more grams during 24 hours. The rapid improvement of the clinical picture corresponds to the laboratory data. The possible uses of this procedure in physiological experiments with respect to carbohydrate and fat metabolism were briefly discussed.

THE DETERMINATION OF VITAMIN C IN URINE.—Kenneth Evelyn, Helga Tait Malloy, and Charles Rosen. (Abstract of paper read on March 21, 1938).

The excretion of ascorbic acid in the urine of normal individuals was studied with the photoelectric method of Rosen and Evelyn (*Trans. Roy. Soc. Can.*, 1937). It was found that the values obtained by visual titration with 2,6 dichlorophenolindophenol were from 2 to more than 10 times too high in some urines, because the visual method failed to differentiate between ascorbic acid and other substances which reduce the indicator at a slightly lower rate. Many normal persons excreted only 1 to 4 mg. of true ascorbic acid per 24 hours, although values of the order of 10 to 20 mg. were obtained by titration. At high levels of excretion however, the discrepancy between the results of the two methods became negligible. No advantage was gained by purifying the urine by the mercuric acetate procedure of Emmerie and van Eekelen, because in the majority of cases a study of the reaction velocity curves showed that the filtrates obtained by this method were almost as badly contaminated with interfering substances as the original urine. This is apparently due to the fact that

* It is published in full in the *Bulletin of the Montreal Medico-Chirurgical Society*.

the mercuric acetate removes some of the interfering substances, while the treatment with hydrogen sulphide produces others by reduction of substances which were present in the original urine in the oxidized state.

ADAPTATION ENERGY.—Hans Selye. (From the Department of Anatomy, Histology and Embryology, McGill University; abstract of paper read on April 25, 1938).

Animal experiments show that continuous exposure to a constant damaging stimulus (cold, excessive muscular exercise, drugs, etc.) elicits a characteristic three stage reaction. During the first stage, the animals are obviously damaged but after two or three days their condition improves in spite of continued treatment with the damaging agent. After a longer period of such treatment the animals lose their acquired adaptation and their condition turns for the worse. This response which is independent of the damaging agent used, and appears to be the somatic expression of adaptation as such, has been termed "the general adaptation syndrome" and its three stages: (1) the stage of the "alarm reaction"; (2) the stage of resistance; and (3) the stage of exhaustion.

The fasting blood sugar which, following a short initial rise, decreases to hypoglycæmic levels during the alarm reaction, increases above normal during the stage of resistance and shows a second fall to convulsive levels during the stage of exhaustion. The blood chlorides and blood volume curves roughly parallel the blood sugar curve.

As a possible explanation of these findings it is suggested that the organism possesses a certain limited amount of adaptability or "adaptation energy" which is mobilized during the alarm reaction and consumed during the stage of resistance, so that the stage of exhaustion would result from the depletion of all the available "adaption energy".

THE THERMOSTABLE METABOLIC STIMULANT IN PITUITARY EXTRACTS AND ITS RELATION TO THE MELANOPHORE-EXPANDING HORMONE.—D. K. O'Donovan and J. B. Collip. (From the Department of Biochemistry, McGill University; abstract of paper read on April 25, 1938).

Further study of the active principle in pituitary extracts which causes an immediate but transitory increase in oxygen consumption showed that it is absorbed by charcoal, and destroyed by tryptic but not by peptic digestion. It is resistant to the temperature of the boiling-water bath at pH 11 for 15 minutes. It is present in highest concentration in extracts of the pars intermedia and pituitary colloid and to a less extent in both anterior and posterior lobe extracts. The melanophore-expanding activity of extracts is approximately proportional to the activity on gaseous metabolism of rabbits.

After intravenous injection into rabbits, weighing 2 to 2.4 kg., of 30,000 melanophore units, defined as the minimal amount which will cause well-marked effects on the intact frog, the respiratory quotient decreased during the first two hours from 0.95 in non-fasted animals to 0.81, and to 0.78 at the 2 to 4 hour period. The oxygen consumption increased +17 per cent and +28 per cent respectively. The CO_2 combining power of the plasma altered slightly (-3.5 c.c. per cent). In animals fasted 24 to 48 hours the fall in R.Q. after injection was relatively slight, from 0.79 to 0.75 in the first four hours, with a 24 per cent increase in oxygen consumption. Controls obtained with adrenalin in doses of 0.5 to 1 mg. subcutaneously showed no significant fall in R.Q.

From a study of carbohydrate stores and nitrogen excretion as well as the tendency to a fall in blood urea it is suggested that the pituitary fraction stimulates fat metabolism and to some extent depresses carbohydrate and protein metabolism.

In conjunction with the results of co-workers, it is possible that the following effects produced by pituitary extracts are caused by a single active principle: melanophore expansion in frogs, calorogenic and R.Q. lowering effects on rabbits, the anti-insulin and anti-adrenalin effects on blood sugar of rabbits, and the ketogenic effect on fasted rats.

THE KETOGENIC AND ANTI-INSULIN EFFECT OF PITUITARY EXTRACT.—A. H. Neufeld and J. B. Collip. (From the Department of Biochemistry, McGill University; abstract of paper read on April 25, 1938).

By using the ketonæmia of treated fasted rats as an index of ketogenic activity of anterior pituitary preparations, we have demonstrated a definite ketogenic activity in a simple aqueous extract (pH 5) of dehydrated and defatted anterior lobes after 15 minutes in a boiling-water bath at pH 11. A similar positive effect was obtained in adrenalectomized rats, although our results on ketonuria in such animals agree with those of Long.* This heat-treated extract also antagonizes the hypoglycæmic action of insulin. It appears unlikely, however, that this insulin antagonism is caused by a secretion of epinephrine, since such preparations also antagonize epinephrine hyperglycæmia. The administration of the heat-treated extract to 4 normal rabbits, either subcutaneously or intravenously, produced a very slight degree of hyperglycæmia in 3 animals. On the other hand, in 4 animals, following a 16 hour fast, 2 showed a mild hyperglycæmic response; whilst in 9 animals

* Long, C. N. H.: Harvey Lectures, 1936-37, pp. 194-228.

following a 24 hour fast, only 1 showed any elevation of blood sugar level.

A posterior pituitary extract prepared according to the directions of the American Pharmacopœia, heated on a boiling-water bath for 1 hour at pH 7 and finally for 10 minutes at pH 11, antagonized both insulin hypoglycæmia and epinephrine hyperglycæmia. Thus it would appear that the anti-insulin and anti-epinephrine factors in posterior and anterior lobe extracts may be identical.

In the pancreatectomized-hypophysectomized dog, kept on a controlled food intake, the heat-treated pituitary preparation produced a marked increase in both the glycosuria and the ketonuria.

The properties of this pituitary factor, such as inactivation by trypsin, stability to heat and alkali, and others, suggest a close relationship to the melanophore-expanding hormone of the pars intermedia. This is further supported by the finding that 1 mg. of a purified melanophore preparation, kindly supplied by Dr. R. L. Stehle, of the Department of Pharmacology, McGill University, produced in fasted rats a marked ketonæmia between the second and the third hours following its administration.

ELECTRO-DIALYSIS OF PITUITARY EXTRACT.—O. F. Denstedt and J. B. Collip. (Abstract of a paper read on April 25, 1938).

Dialysates of dilute acid extracts having a high melanophore hormone content have produced the following physiological effects: (1) antagonism to the hypoglycæmic action of insulin in the rabbit; (2) antagonism to the hyperglycæmic action of adrenaline in the rabbit; (3) increase in oxygen-consumption and lowering of the R.Q. in the rabbit; (4) production of ketonæmia in the fasted rat.

The possibility that all of these effects are due to one hormone has to be considered.

On electro-dialysis the active principle or principles may be recovered almost completely in the cathode dialysate, a relatively negligible amount being found in the anode compartment and in the dialyzed residue. The hormone is readily absorbed by acid earths. Heating extracts with 0.25 N. acid or alkali may cause a potentiation in melanophore activity but prolonged heating causes inactivation.

Under the conditions of our experiments we have found that the growth, adrenotropic and gonadatropic principles are not recovered in dialysates when either cellophane or collodion are used as membranes.

In preliminary experiments with fish-bladder membranes a considerable amount of thyreotropic principle has been obtained in the cathode cell. Experiments are now in progress using the electrophoretic principle of separating the various pituitary factors.

SOME EFFECTS OF SEX HORMONES ON CERTAIN ABNORMALITIES OF CORPUS LUTEUM FUNCTION (Metropathia hæmorrhagica and secondary amenorrhœa).—J. S. L. Browne. (Abstract of paper read on October 8, 1937).

It has been found that the following method of therapy with progesterone is of benefit in the treatment of those cases of metropathia hæmorrhagica which show cystic glandular hyperplasia in the endometrium. A therapeutic curettage is first performed. If this is not done there is a tendency for profuse bleeding to follow the giving of progesterone. Two weeks after this four intramuscular injections of 5 mg. (5 rabbit units) of progesterone are given, one every other day. Bleeding generally follows in from one to four days after the last injection and is usually normal in amount and duration. The next series of injections is commenced 20 days after the beginning of this bleeding: if this is done the next bleeding will occur 28 to 30 days after the last bleeding. It is questionable how long an interval of amenorrhœa it is safe to allow between the periods of bleeding without incurring the danger of recurrence of profuse bleeding. The length of the interval can be determined by the time at which the progesterone injections are begun and stopped. One case has been carried on for 28 and one for 19 periods of bleeding at from 22 to 30 day intervals. In these two cases when the injections were not given no bleeding occurred in one case for 57 days and in the other for 45 days: progesterone injections were then started and bleeding occurred on the 66th day after the last bleeding in the first case and on the 52nd day in the other. If the anæmia is marked it is always desirable to give adequate doses of iron by mouth; in some cases merely re-establishing a series of normal bleeding periods with progesterone is not followed by a rise in hæmoglobin content of the blood. From the symptomatic point of view the patients are cured. Five other cases have been carried on for a shorter time. The periods of bleeding so artificially produced are not excessive in amount and there is no bleeding in the intervals between them.

Hitherto progesterone has been used to check the bleeding of metropathia hæmorrhagica while it was occurring. The present method of treatment is based on the following theoretical conception. The ovaries in the cases of metropathia hæmorrhagica showing cystic glandular hyperplasia secrete continuously amounts of œstrin which are not necessarily excessive but which act over a long period of time on the endometrium, causing it to become hyperplastic. The injection of progesterone at intervals as described above attempts to reproduce the sequence of events taking place in the normal menstrual cycle, by allowing the œstrin secreted by the patient's ovary to act

for approximately the length of time that it would do in the normal cycle, and then reproducing in part the effect of the formation of a corpus luteum which normally occurs at this time. The doses of progesterone and the length of time over which they are given are inadequate to produce complete progestational transformation of the endometrium; in fact very little histological change is seen. In spite of this, bleeding follows promptly on the cessation of the progesterone injections.

In a further group of cases of secondary amenorrhœa whose endometria show on histological examination a picture similar to that of cystic glandular hyperplasia it has also been possible to bring on a normal period of bleeding repeatedly by giving and withdrawing progesterone in the manner and in the dosage described above.

The Saint John Medical Society

The annual meeting of the Saint John Medical Society was held on May 25th, at which routine business was carried out. Election of officers resulted as follows: *President*, Dr. V. A. Snow, Hampton; *Vice-president*, Dr. G. B. Peat, Saint John; *Secretary*, Dr. Douglas Gibbon, Saint John; *Treasurer*, Dr. Joseph Tanzman, Saint John; *Executive Committee*, Drs. A. E. Macaulay, R. A. H. McKeen and J. P. McInerney, Saint John.

St. Joseph's Hospital, Winnipeg

At a meeting of the staff of St. Joseph's Hospital, Winnipeg, held in the hospital on the evening of May 23rd, with Dr. James McKenty in the chair, Dr. J. R. Davidson gave a review of his research work illustrated with lantern slides. He stated that his attention had been first aroused by the response of a woman suffering from advanced carcinomatosis in the public wards of the Winnipeg General Hospital to a diet rich in vitamins and how life was prolonged for a considerable period as long as she remained on that diet. He then began experimental work on mice and found that the tumour threshold in mice can be raised or lowered by placing them on a diet low or high in vitamins. The experience gained from these experiments had enabled him to use a high vitamin content diet in other patients with advanced malignancy. However, he was convinced that the proper method of attack against cancer was to prevent it by proper diet rather than seeking to cure patients in whom the condition was already established.

At the close a resolution was unanimously passed by the meeting expressing confidence in Dr. Davidson's work and the hope that funds might be made available to enable him to continue with his research. The resolution will be forwarded to the Winnipeg Medical Society.

The Saskatoon and District Medical Association

At a recent meeting of the Saskatoon and District Medical Association Dr. Duncan Croll presented a case of myeloma of the femur in a girl age 10. No treatment is being given. The prognosis is hopeless.

Dr. Lillian Chase, of Regina, gave a paper on "Diabetes with special reference to regulation of protamine zinc insulin dosage". Dr. H. Landa, intern at the Saskatoon City Hospital gave a demonstration of blood sedimentation tests. In discussing this, Dr. G. H. Hames stated that they had done about 10,000 such tests at the Saskatoon Sanatorium and that in his opinion the Schilling test was of more value in estimating whether a new infection had been superimposed upon the old one than the sedimentation test.

LILLIAN A. CHASE

The Winnipeg Medical Society

At the regular annual meeting of the Winnipeg Medical Society held on May 19th, the retiring President, Dr. O. J. Day, gave a most interesting address on "Plagues and pestilences in history". The election of officers for the coming year resulted as follows: *President*, Dr. O. C. Trainor; *Vice-president*, Dr. R. W. Richardson; *Treasurer*, Dr. H. M. Edmison; *Secretary*, Dr. C. B. Stewart; *Trustee*, Dr. Dugald McIntyre.

Post-Graduate Courses

Edinburgh University

An eight weeks' intensive post-graduate course on internal medicine, will be held in Edinburgh, from Monday, October 17, to Saturday, December 10, 1938. The attendance will be limited to thirty-two.

The course will be conducted by the Honorary Staffs of the Royal Infirmary and the various special hospitals. The graduates will be apportioned for ward work to the eight Honorary Physicians on the staff of the Royal Infirmary, four graduates being attached to each charge. There will be four hours' co-ordinated teaching daily throughout the course, the various departments of medicine being dealt with in successive weeks. The course is open to women.

The fee for the course will be fifteen guineas, and entries will be registered in order of application. The Secretary, Post-graduate Courses in Medicine, University New Buildings, Edinburgh 8, Scotland.

The New York Academy of Medicine

The Eleventh Annual Graduate Fortnight of the New York Academy of Medicine will be held from October 24 to November 4, 1938. The subject to be discussed is "Diseases of the blood

and blood-forming organs". The fortnight will present a carefully integrated program which will include clinics and clinical demonstrations at many of the hospitals of New York City, evening addresses, and appropriate exhibits. Twenty-three hospitals have accepted the invitation to participate by having prepared afternoon clinics and clinical demonstrations which will be coordinated with the evening meetings. The evening sessions at the Academy will be addressed by recognized authorities in their special fields, drawn from leading medical centres of the United States. A comprehensive exhibit of books, pathological and research material, diagnosis, treatment, and prevention, whenever possible, clinical and laboratory diagnostic methods, x-rays, action of drugs and other therapeutic measures, will be demonstrated. A complete program and registration blank may be secured by addressing Dr. Mahlon Ashford, the New York Academy of Medicine, 2 East 103rd Street, New York, U.S.A.

University Notes

Dalhousie University

Dalhousie University conferred the degrees of Doctor of Medicine and Master of Surgery on twenty-nine of her graduates at the annual spring convocation. This represented a fraction more than half of the fifty-seven freshmen in medicine of five years ago. The gold medallist was Chester Stewart, of Prince Edward Island. Dr. Stewart has been appointed to the Medical Department of the National Research Council. Through the next few years most of the graduates will be serving as interns in hospitals of eastern and central Canada and the United States.

University of Manitoba

At the annual convocation of the University of Manitoba held on May 18th the following medals were awarded to graduates in medicine: the University Gold Medal, Dr. Ton Lung Quong; the Manitoba Medical Association Gold Medal for the highest standing on the first four years of the course, Dr. Metro Alexander Ogryzlo; the Dr. Charlotte W. Ross Gold Medal for highest standing in obstetrics during the course, Dr. Ton Lung Quong.

The Jubilee Award offered by the Alumni Association of the University of Manitoba for services of outstanding and permanent benefit to the extra-curricular life of the University, Dr. W. Donald Ross, B.Sc. (Med.); the Chown Prize in Medicine, (established by the Faculty of Manitoba Medical College as a tribute to their former Dean, Dr. H. H. Chown, and awarded each year to the two students of the graduating class having the best aggregate standing on the

subjects of medicine and surgery, respectively, throughout the course). Medicine, William Locke, Gold Medal and \$50.00; surgery, William Kenneth Massey, B.A., Gold Medal and \$50.00. The Prowse Prize for Research in Medicine (offered annually for an original investigation in any department of medicine, clinical or laboratory, judged upon the basis of scientific quality of work and validity of conclusions to be of sufficient merit; open to fourth and fifth year undergraduates and to graduates of not more than ten years' standing), Murray Hogg Campbell, M.D., Bronze Medal and \$25.00.

At a meeting of the Faculty Council of the Faculty of Medicine, University of Manitoba, Dr. Ross Mitchell was appointed representative on the Senate of the University for two years.

McGill University

Ninety-five candidates received the degree of M.D., C.M., at the Convocation held on May 26, 1938. Their names are as follows: Earle H. Anderson, B.Sc., Digby, N.S.; William S. Bagnall, A.B., Richmond, Cal.; Charles M. Barbour, A.B., Newport, Me.; Robert G. Baxter, B.Sc., St. Lambert; Marshall R. Beard, Sacramento, Cal.; Harvey C. Boyd, A.B., Ann Arbor, Mich.; Theodore A. Breton, B.A., Sault Ste. Marie, Ont.; J. Robert Brooke, B.Sc., Seattle, Wash.; John H. Buell, New Haven, Conn.; Arthur F. Chaisson, M.A., Saint John, N.B.; Frederic D. Chapman, A.B., Syracuse, N.Y.; William F. Chapman, A.B., Broadalbin, N.Y.; C. Leland Colm, Durham, Cal.; Raymond L. Conklin, M.Sc., Macdonald College, Que.; J. Bernard Cook, B.A., Sudbury, Ont.; Lincoln W. Cromwell, Burnaby, B.C.; Everett F. Crutchlow, B.A., Westmount; Milton L. Cullen, A.B., Mattapan, Mass.; Allister L. Cunningham, Glace Bay, N.S.; William R. Duncan (*in absentia*), Seattle, Wash.; Vernon M. Dunfield, B.A., Bayfield, N.B.; Mordecai Etzioni, B.A., Montreal; Kenneth A. Evelyn, B.Sc., Jamaica, B.W.I.; Francis P. Flood, B.A., Montreal; Simon A. Flynn, B.A., Holyoke, Mass.; George E. Foster, B.A., Fredericton, N.B.; Norman E. Foster, Abernethy, Sask.; Alex. M. Fraser, M.A., Scotstown, N.S.; Hugh W. Garol, B.A., San Francisco, Cal.; William C. Gillick, Niagara Falls, N.Y.; Eugene G. Gormley, B.S., Lancaster, N.H.; Arden R. Hedge, San Francisco, Cal.; Gordon M. Hemmett, A.B., Glens Falls, N.Y.; E. Rowland Henderson, B.A., Lachine, Que.; James H. B. Hilton, Ottawa, Ont.; George R. Hornig, B.Sc., Brooklyn, N.Y.; George R. Howell, Westmount; Ralph H. Huff, A.B., Huntingdon, N.Y.; Frank J. Hughes, M.Sc., Gloucester, N.J.; Frederick R. Jardine, Kensington, P.E.I.; Constantine H. Kapp, Winston-Salem, N.C.; Eli I. Katz, Montreal; Joseph C. Kelly, B.Sc., Ogdensburg, N.Y.; Edward E. Kemble, Erie, Pa.; Jacob H. King, Broad Cove,

Nfld.; George E. Kirk, Ph.B., No. Providence, R.I.; Horace H. Koessler, B.Sc., Seeley Lake, Mont.; John F. Lake, Columbus, Ohio; Roland E. Lapointe, B.Sc., Manchester, N.H.; Joseph G. LeBrun, B.A., Montreal; Herman Levin, B.Sc., Westmount; George W. Lilley, Chester, Pa.; John B. Lynch, B.A., Sydney, N.S.; W. J. Campbell MacArthur, Winnipeg, Man.; Wilfred D. McCusker, B.Sc., Bismarck, N.D.; Michael R. MacDonald, B.Sc., Sydney Mines, N.S.; John E. McGovern, B.A., Westmount; Richard D. McKenna, B.A., Westmount; Kenneth R. Mackenzie, B.A., Montreal; James Gordon McLeod, B.Sc., Regina, Sask.; Joseph A. McMillan, B.Sc., Charlottetown, P.E.I.; Salvatore Maneuso, Montreal; Benjamin R. Maxwell, Hopewell, N.S.; Gerald V. Mitchell, Winstead, Conn.; Henry G. Morgan, B.A., Hollywood, Cal.; Harry L. Nutik, B.Com., Montreal; Paul M. Osmun, A.B., Netcong, N.J.; Felix Peebles, B.Sc., Jefferson, Texas; Edward R. Peterson, Saskatoon, Sask.; Henry M. Pickard, Wilmington, N.C.; Harold E. Pittis, B.A. (*in absentia*), Lakehurst, N.J.; Robert Wm. Quinn, Eureka, Cal.; E. William Reitor, Nevada City, Cal.; Thomas H. Richert, B.A., Pacific Beach, Cal.; Carroll A. Russell, Watonsville, Cal.; Michael J. Sabia, B.Sc., Hamilton, Ont.; George P. Sayre, A.B., Essex Falls, N.J.; Isadore Sedlezky, Montreal; Reuben I. Seime, B.Sc., Viroqua, Wis.; Philip H. Sheridan, B.Ph., Blackstone, Mass.; Samuel Silver, Montreal; Israel J. Simburg, B.Sc., Vegreville, Alta.; Albert B. Smith, B.S. (*in absentia*), Norwich, N.Y.; A. Macrae Smith, B.S., Bellingham, Wash.; Howard P. Snyder, Bound Brook, N.J.; Robert B. Somerville, Bristol, N.B.; John D. Stenstrom, Westmount; Arthur J. Stewart, B.A., Prince Rupert, B.C.; Archibald C. Stone, Chatham, Ont.; Ernest J. Talbot, B.A., Valleyfield, Que.; Charles A. Thompson, B.A., London, Ont.; Arthur J. Tillinghast, Hackensack, N.J.; Robert J. J. Tipler, B.Sc., Chicago, Ill.; John T. Wright, B.Sc., Reno Nev.; Cuthbert R. Yolton, Massena, N.Y.

The prize winners are: Joseph A. McMillan, Holmes Gold Medal for the highest aggregate in all subjects forming the Medical Curriculum, the Lieutenant-Governor's Silver Medal for the highest standing in Public Health and Preventive Medicine, the Jeanie Forsyth Prize for high standing in Surgery; Kenneth A. Evelyn, Wood Gold Medal for the best clinical examinations in the subjects of the final year; James H. B. Hilton, the Alexander D. Stewart Memorial Prize for the highest general qualifications for the Practice of Medicine.

University of Toronto

Medals, prizes, fellowships, scholarships and bursaries awarded by the Senate of the University, Faculty of Medicine.

Sixth year.—The Faculty Gold Medal, A. Goggio, B.A.; the Faculty Silver Medal, E. B.

Tovee; the Faculty Silver Medal, M. E. Borsook; the Ellen Mickle Fellowship, A. Goggio, B.A.; the Chappell Prize in Clinical Medicine, A. F. Goggio, B.A.; the William John Hendry Memorial Scholarship in Obstetrics and Gynaecology, W. E. Apted; the Ontario Medical Association Prize in Preventive Medicine, E. B. Tovee; the David Dunlap Memorial Scholarship, A. A. K. Bochner.

Undergraduate.—The David Dunlap Memorial Scholarships: (a) fifth year, D. H. Copp, B.A.; (b) third year, G. R. Walker and B. Winter; the Ronald S. Saddington Medal in Pathology, T. A. Fraser, M.A.; the James H. Richardson Research Fellowship in Anatomy, F. Richardson, M.B., B.S. (Lond.); the Toronto Women's League of the United Synagogue, H. H. Fireman.

Graduate.—The Reeve Prize, C. G. Smith, M.Sc. (West.), B.A., M.D., Ph.D. (Tor.); the Starr Gold Medal, M. O. Klotz, M.D.; the Alexander McPhedran Research Fellowship in Clinical Medicine, J. L. A. Fowler, M.D.; the Perry Goldsmith Prize in Oto-laryngology, G. W. McGregor, M.B.; the J. J. Mackenzie Fellowship in Pathology and Bacteriology, C. L. Burke, B.A., M.D.

The University of Western Ontario

At the convocation held on June 1, 1938, the degree of Doctor of Laws (*honoris causa*) was conferred on Dr. Henry A. Christian. Hersey Professor of the Theory and Practice of Physic, Harvard University.

The degree of M.D. was conferred on the following 33 candidates: F. S. Babb, G. R. Bourne, F. D. Brent, W. J. F. Bugg, J. J. Carroll, W. F. Copp, W. E. Crysler, S. D. Ellman, Grace Frank, P. G. Gettas, A. G. Ginsberg, Sonya Hoffman, H. J. D. Jay, G. E. Jenkins, C. R. Kemp, H. N. Kittenplan, H. J. Lipson, S. Luria, J. D. C. Macdonald, D. L. McRae, S. J. C. Miller, J. D. Munn, H. T. Norry, E. R. Patterson, N. Pollack, D. M. Sharpe, B. E. Sherk, F. H. Smith, H. A. Snell, W. J. Tighe, J. B. Tindall, A. B. F. Vogelsang, A. Wilensky.

Prizes and scholarships were awarded as follows: the Alpha Kappa Kappa Gold Medal, S. J. C. Miller; the J. B. Campbell Memorial Scholarship in Medicine, W. J. Tighe; the Class of 1917 Scholarship, W. E. Crysler; the W. J. Roche Scholarship, F. H. Smith; the Ontario Medical Association Scholarship in Preventive Medicine, S. J. C. Miller; the Khaki University and Y.M.C.A. Scholarship, D. L. McRae.

Letters, Notes and Queries

Professor Rudolf's Article "Post Hoc Ergo Propter Hoc"

Dr. C. E. Douglas, St. Andrews, Fife, Scotland, writes to the author appreciatively of this article, which appeared in the *Journal* recently (1938, 38: 281). In part, he says.

"I have read it with much interest. Your very first instance of the pneumonia brought on by winning a prize in the Irish Sweepstake reminded me of a case in point, only it was one of D.T. My patient was an excellent fellow, but rather convivial in habit, and I had often told him that he need never be ill if he would leave off the drink, which he did for 18 months; after which I was rung up by his wife: D.T. again. Treated *secundum artem* he soon came round, when we discussed the cause of this lapse. Whereupon the wife let the cat out of the bag. He had drawn a starter for the Calcutta Cup, got a cheque for £90, cashed it, and drank it off with his boon companions! Quite a parallel case to your pneumonia!

Of course we are prone to take for granted that our treatment has brought about recovery (and sometimes people are prone to take the same view if the patient dies), but one must allow for the frailty of human nature, and perhaps this frailty is not all to the bad; if we were all strictly logical what a dreadful world it would be. However, my point is that I enjoyed your pleasantly erudite paper and thank you very much for sending it to me."

May 20, 1938.

The Care of the Hypodermic Syringe

No one will deny that the hypodermic syringe is one of the most important weapons in the doctor's armamentarium. Some may even think that its use is so thoroughly understood that it is the work of supererogation to discuss it. There are, however, a few points in its management which will bear emphasizing, even to a generation which is so familiar with its employment. It would be superfluous to labour the need for absolute asepsis, a lesson of the medical student's cradle. That this lesson has been thoroughly learnt is proved by the rarity of sepsis as a result of hypodermic medication. The next point is the advisability of causing the minimum of pain. Patients do not like being hurt, and here two considerations must be borne in mind. The needle must be the finest possible and irreproachably sharp. It is not very difficult to keep a needle sharp provided that care is taken not to boil it for long periods. Needles must be boiled, but they should only be

immersed for a few seconds at a time. In these days it is more expensive to have needles re-sharpened than to buy new ones, which luckily are quite cheap, and if there is an extravagance which is pardonable on the part of a doctor it is in keeping himself well supplied with hypodermic needles of blameless acuity. Oily and viscous solutions, which are not readily drawn up into a narrow tube, often have to be injected through a needle of fine bore. But when such a solution is once introduced into the barrel of the syringe it can be forced out through a comparatively fine needle if sufficient finger pressure is supplied to the piston. For this reason it is often advisable for filling purposes to detach the needle, dip into the oily solution the glass nozzle, and draw the oil straight up into the barrel: after which the needle can be replaced and the desired dose administered through it. But care must be taken in doing this to hold the base of the needle with the finger and thumb firmly against the glass nozzle so that the firm pressure needed to force the oil through the narrow metal tube does not cause it to part company with the barrel, thus wasting the contents. From time to time one hears of cases where the needle breaks off and the distal portion becomes buried under the patient's skin. This accident, which has been known to lead to legal proceedings, is not really difficult to avoid. Fracture of the needle always takes place at its junction to the base. This is where corrosion is liable to set in, and is another argument for never using the same needle too long and too often; but in any case the danger of burying the needle in the patient can always be avoided by taking care not to plunge it in right up to the hilt. Provided this precaution is taken, even if the needle should break there will be a projecting portion which can easily be grasped and drawn out. As regards the care of the glass barrel of the hypodermic syringe, the chief risk to its integrity occurs during the frequent boilings to which it must be subjected. The risk becomes much increased in the case of large syringes such as are used more and more nowadays for intravenous injections. Heat-resisting glass has been introduced for this reason, but syringes constructed of this material are much more expensive than others, and the life of ordinary glass barrels is much prolonged if care be taken to keep them from resting on the bottom of the sterilizer. Everyone knows that the barrel should never be boiled with the piston *in situ*, and it is a good plan to support the barrel, and the piston also if made of glass, in the metal frame invariably supplied by the makers for holding them in their case. This ensures that the whole barrel is heated evenly and does not bump on the bottom of the sterilizer. It need hardly be said that the barrel of the syringe should be carefully cleaned every time it is used, but this is not always quite easy.

Some of the solutions and emulsions for which it may be employed are liable to leave adherent deposits behind them. A great deal can be done with a pledget of cotton-wool grasped in a pair of fine forceps, but even this is not always adequate to remove the last traces of a mercurial or bismuth cream. In such cases an efficient cleansing may usually be obtained by passing either benzine or petrol through the syringe, afterwards removing all traces of it with methylated spirit.—From *Brit. M. J.*

Sterilization of Hypodermic Syringes

Sir.—In the *Journal* of April 30 (p. 955) there is an annotation referring to the sterilization of hypodermic syringes. I would like to describe a method I have used for over thirty years, never seeing any sign of sepsis after an injection. I was taught by Sir Almroth Wright to sterilize the syringe with boiling olive oil in the following way. Have in a small crucible half an ounce of olive oil and a tiny crumb of bread. Put a spirit lamp underneath and boil till the crumb turns brown. Then fill the syringe full, avoiding the crumb. Do this no more than twice, or the solder holding the nozzle to the glass barrel will melt. Sir Almroth Wright told me that the heat of boiling oil will kill all spores as well as germs.

The next point is the use of a platinum needle, which may cost 7s. 6d. but with care lasts for a year. When about to give an injection all that is required is to draw the needle through the spirit lamp flame. The needle becomes red hot, and is then ready to suck up the vaccine or other solution. I have always used a Record syringe in a metal case that takes the syringe with the needle left on. When going out on a visiting round I measured my dose in the syringe, boiled a drachm of water in the metal case, poured it out, and replaced the syringe in the case. It was then ready for use. If by chance I touched the needle on anything it was quite easy to put the platinum needle through a flame. There is no need, in my experience, to use the boiling oil in the syringe more often than once a week if the needle is kept on the nozzle. There must be hundreds of men who were trained by Sir Almroth Wright in his method of syringe sterilization. Why they persist in using the messy, elaborate boiling water method with steel needles passes my comprehension.—J. Sandison Crabbe, in *Brit. M. J.*, 1938, 1: 1070.

Poison Ivy

To the Editor:

If any of your Montreal readers wish to refresh themselves on the appearance of poison ivy, it can be done, readily, within 300 yards of the Western Division of the Montreal General Hospital, on the lane between Selby Street and the C.P.R. right of way, just west of Atwater

Avenue. There is a whole hedge of it hanging over the wall. Today, I collected a long piece with my gloved hand without leaving my car. It can be readily identified by the clusters of three leaves. The leaves resemble those of Virginia Creeper, which, however, occur in clusters of five. (Safety lies in five). By the time this is in print there will be clusters of small shot-sized dun coloured berries, each containing twelve to twenty berries. The children of Selby Street are well aware of its presence, as about fifty of them were treated in the Western Division Out-Patient Department for dermatitis during the summer of 1937.

The C.P.R. at the request of the Westmount Health Officer sent some men to eradicate it last year, but this weed thrives on the treatment it received. If it is to be properly extirpated radical treatment will be necessary. This pest is rapidly spreading over the whole Island of Montreal, and if persistent efforts are not carried out dermatologists will be overworked.

Montreal,
May 31, 1938.

C. R. BOURNE.

Topics of Current Interest

Poliomyelitis Infectivity of Human Stools

The recent isolation of the virus of poliomyelitis from human faeces¹ is presumably additional evidence that viable virus can pass through the gastrointestinal tract. There is as yet no experimental evidence that this virus proliferates in the intestine. Nevertheless, identification of the virus in human stools suggests that certain precautions should be taken that are now generally considered unnecessary.

Following the successful transmission of poliomyelitis to monkeys, tests were made as early as 1912 of the infectivity of faecal poliomyelitic material. Kling, Pettersson and Wernstedt,² of Stockholm, reported the successful inoculation of monkeys by the intracerebral injection of colonic washings from infants during both the acute and the convalescent period of infantile paralysis. This result was confirmed three years later by Sawyer.³ Since lethal paralytic effects can be produced by control intracerebral injection of normal faecal extracts, this earlier apparently successful isolation and identification of the virus in human stools was generally discredited.

Last year, Harmon⁴ repeated these early tests

1. TRASK, J. D., VIGNEC, A. J. AND PAUL, J. R.: *Proc. Soc. Exper. Biol. & Med.*, 1938, 38: 147.
2. KLING, C., PETTERSSON, ALFRED AND WERNSTEDT, W.: *Communications Inst. méd. Etat Stockholm*, 1912, 3: 5.
3. SAWYER, W. A.: *Am. J. Trop. Dis. & Prev. Med.*, 1915, 3: 164.
4. HARMON, P. H.: The use of chemicals as nasal sprays in the prophylaxis of poliomyelitis in man, *J. Am. M. Ass.*, 1937, 109: 1061.

under adequately controlled conditions and was able to isolate and identify poliomyelitis virus in the stools of four of twenty patients tested. The most convincing evidence of intestinal infectivity, however, is currently reported by Dr. J. D. Trask¹ and his co-workers of the department of paediatrics at Yale University. The Yale paediatricians tested faecal infectivity by the less toxic method of intraperitoneal injection in monkeys. In their technique 120 c.c. of distilled water were added to the whole stool of the infant and the mixture agitated and allowed to stand for two hours at room temperature. The supernatant fluid (90 c.c.) was then pipetted off into a rubber stoppered flask and partially sterilized by the addition of 15 per cent ether (U.S.P.). After storage for twenty-four hours at refrigerator temperature, 30 c.c. of the etherized supernatant fluid was injected intraperitoneally into monkeys. As an alternate method the ether was removed and the fluid reduced to about a tenth of its original volume by vacuum distillation. This concentrate was also to be used for control intracerebral injections. Of the eleven monkeys thus far injected intraperitoneally with the etherized supernate but one developed peritonitis and bacteraemia.

By this intraperitoneal technique the Yale paediatricians successfully recovered viable poliomyelitis virus from the stools of an 18 months old infant on the second, fourteenth and twenty-fifth days of the disease. Monkeys thus inoculated usually had typical paralytic symptoms on the seventh day. Paralytic symptoms and histological lesions were characteristic of experimental poliomyelitis in this animal. Successful passage to a second monkey was accomplished by routine techniques. Additional work must be done, however, before a final interpretation of these results is possible.—*J. Am. M. Ass.*, 1938, 110.

Interference with Wireless Reception by Electro-medical Apparatus

At the suggestion of the Postmaster-General the Minister of Health has issued a circular letter to local authorities (No. 1695), enclosing a memorandum on the prevention of interference with radio reception from certain types of electro-medical apparatus. A leading article on this subject appeared in the *British Medical Journal* of April 9, 1938, p. 786. The memorandum was prepared by the Radio Branch of the General Post Office, and its purport has already been brought to the notice of the principal voluntary hospitals in this country, through the British Hospitals Association, in the issue of *The Hospital* for September, 1937. The memorandum is primarily concerned with certain types of diathermy installations working on medium waves, short waves, and ultra-short waves.

ELECTRICAL SCREENING OF ROOMS

Radio receivers situated at up to one mile or more from the electro-medical apparatus may be affected, so that a single apparatus may affect a very large number of receivers. The radio services which may be affected are not only the B.B.C. broadcast and television transmissions on long, medium, or ultra-short waves, but also Government services, Air Force, civil aircraft, police, shipping, and other commercial services, in some of which the safety of life on land, at sea, and in the air may be involved.

The interference may reach a radio receiver by two means—either by conduction from the source along the electric supply mains, from which it is eventually radiated to the aerial, or by radiation from the source directly to the radio receiving aerial. The former method of propagation is known as "mains-borne", the latter as "direct radiation". Mains-borne interference can be suppressed by connecting in the mains supply to the diathermy apparatus a suitable filter consisting of condensers and/or radio frequency inductors ("chokes"). Directly radiated interference can only be suppressed by enclosing in an electrical screen or Faraday cage not only the apparatus but also the patient and the operator. This is not practicable in the case of the mobile ward unit, but may be applied to the considerably more common case in which the bulk of the treatment is given in one room set apart for the purpose. This latter case is the one which in practice gives rise to the large majority of complaints of interference with radio reception.

It is obviously undesirable to enclose the apparatus, patient, and operator in a closely fitting screen, and the methods of screening which have been developed by the G.P.O. Radio Branch rely on fitting the screening material to the surfaces which enclose the room in which treatment is given. Two methods in particular have been developed, one primarily for dealing with an existing room, the other for application to a building which is in course of erection. In the former case metallized paper is applied to the walls, doors, and ceiling of the room above the plaster, the floor being covered with either heavy-gauge metallized paper or else with quarter-inch wire netting. The floor screening material is covered by linoleum or other floor covering. The recommended type of metallized paper consists of aluminium foil (not sprayed aluminium or aluminium paint) supported on a paper backing. The windows are covered with wire netting.

It is desirable that provision should be made, in any new hospitals or extensions to existing hospital buildings in which apparatus of this kind is likely to be used, for the inclusion of screened rooms of the type outlined in the memorandum. The Radio Branch of the General Post Office is prepared to advise on any problems arising in the provision of screened rooms for future installations, as well as on the prevention of interference which may be found to be caused by existing plant.

Pending further consideration of the important question discussed in our leading article regarding the suitability of certain wave-bands which might be reserved for the users of electro-medical apparatus, the Secretary of the British Medical Association would like to have as much information as possible from members possessing expert knowledge.—*Brit. M. J.*, 1938, 1: 1063.

Air-conditioning

For the first time in the history of the fast growing air-conditioning industry the buying public will be offered definite protection against the installation of equipment improperly designed to do the job expected of it or represented to perform all of the functions of air-conditioning, when in reality only a partial service will result. A "Code of Minimum Requirements for Comfort Air-Conditioning" just adopted by the American Society of Heating and Ventilating Engineers, and developed jointly with the American Society of Refrigerating Engineers, has set up a uniform procedure for establishing the fundamental basis for the design of comfort conditioning installations. In the making for the past two years its sponsors aim at establishing minimum design standards by which purchasers can judge the performance of equipment. While voluntary in nature, it is hoped the code will discourage sale of spurious apparatus under the guise that it is air-conditioning.

For winter air-conditioning, 70° indoor temperature with 35 per cent relative humidity when outdoor temperature is 30° is set as a minimum design standard. For summer air-conditioning an indoor design schedule of "effective temperatures" (which are index of comfort based on a combination of temperature, relative humidity and air motion) is established, ranging from 71° "effective temperature" when it is 80° outside to 75.5° "effective temperature" when it is 105° outdoors.

The code specifies the introduction of outside air for ventilating purposes at a rate of not less than 10 cubic feet per hour, per occupant, or not less than 15 cubic feet in premises where smoking is permitted, with removal of 95 per cent of ordinary dust particles to provide requisite air purity.

Air velocities, which account for drafts and are a frequent cause of complaint in air-conditioning systems, are limited to not more than 50 linear feet per minute, according to the new code. Control of air temperatures within 3° at the five foot level or the "breathing zone" are also specified in the code.—The American Society of Heating and Ventilating Engineers.

TWINS, TRIPLETS, AND QUADRUPLETS.—The United States has no living quintuplets, but six sets of quadruplets were born there in 1936, according to figures of the U.S. Census Bureau. In four of the sets all babies lived. In 1936, there were reported 232 sets of triplets in which all three are living; 29 sets in which 2 of the 3 babies in each set lived; and 16 sets in which one baby of each set lived. The reports show 22,760 sets of twins with both babies living, and 1,809 sets with one twin surviving in each set. The total number of live births for 1936, the latest year on which complete figures are available, was 2,144,790. Of these, 2,096,667 were single births, the rest being either twins, triplets, or quadruplets.

Abstracts from Current Literature

Medicine

Over-stimulation of the Vagus Nerve in Rheumatic Fever. Keith, J. D.: *Quart. J. Med.*, 1938, 7: 29.

It is well established that the conduction time between the auricular and ventricular nodes is frequently lengthened in rheumatic fever. This disturbance of conduction (as shown in lengthening of the P-R interval) is so common that some observers have even suggested that in young persons excessive lengthening of the P-R interval is diagnostic of rheumatic fever, provided syphilis is ruled out. In the present paper Dr. Keith has reviewed a large number of cases of rheumatic fever of all types. He first shows that the apparent severity of the attack has little relation to the degree of disturbance of conduction. A minimal cardiac lesion as shown clinically may show a marked increase in the P-R interval.

What causes this disturbance in conduction in this disease? The most widely accepted theory is that it is cellular infiltration of the auricular-ventricular node and surrounding tissues, and oedema. Such localized pathological changes are thought to be due to spread of the disease process from the root of the aorta, and to compression of the cells in the bundle tissue by oedema, where it is surrounded by the rigid structure of the septum. This explains the severe cases, but it is not so convincing in the mild cases in which there is no evidence of aortic lesions, and oedema of the bundle is unlikely.

The same objection may be applied to the theory that the conduction is slowed by toxins, unless these are specific for the heart. But it is admitted that possibly the mechanism controlling conduction is unusually sensitive in children.

The suggestion made is that this disturbed condition is due to over-stimulation of the vagus. What causes this is another question, but it is suggested that it is an abnormality at the termination of the vagus in the heart rather than in the medulla. It is significant that the most abundant vagal nerve supply in the heart occurs in the regions where there is such a high incidence of pathological change in rheumatic fever, i.e., the left auricle, the pulmonary and aortic roots, the arteries, and the auriculo-ventricular node. H. E. MACDERMOT

The Sedimentary Rate in Angina Pectoris and Coronary Thrombosis. Riseman, J. E. F. and Brown, M. G.: *Am. J. M. Sc.*, 1937, 194: 392.

The rate of sedimentation of red blood cells is increased in the presence of tissue damage or infection. Coronary thrombosis and its myocardial infarction can be shown to have a more

rapid rate than angina pectoris. A normal or only slightly increased rate on the fourth to twelfth day after an acute cardiac episode is good evidence against coronary thrombosis. The test is of no value in differentiating gall-bladder disease.

The elevation of the sedimentation rate is one of the most constant manifestations of coronary thrombosis, especially within the first fortnight. The progress of the patient is reflected in the sedimentation rate, and rest in bed is indicated until the rate is normal or stationary for three weeks.

The mortality in patients with fast sedimentation rates was found to be double that of those with normal rates.

C. R. BOURNE

Surgery

Cerebral Pneumography. Hyndman, O. R.: *Arch. Surg.*, 1938, 36: 245.

Cerebral pneumography was introduced by W. E. Dandy, and first described by him in 1918. The use of the pneumogram in diagnosis made it possible to transform what would be for many patients an exploration of the brain into an exploration of the pathological conditions of the brain. The author has adopted the policy of attempting to fill the ventricular spaces completely with air, so as to obtain as complete a ventriculogram as possible under the circumstances. He does not limit it to patients with so-called silent tumour, but prefers it as a preliminary measure where neurological examination provides data of localizing value. He gives illustrative case-records where cerebral pneumography had been used in meningeal fibroblastoma, chronic subdural hæmatoma, ependymoma, cystic astrocytoma, angioma, tumours in and about the third ventricle, the thalamus, of the pineal body, of the quadrigeminal plate, of the cerebellar vermis, of the foramen of Magendie. He states that in an experience with 250 ventriculograms he has been successful except in possibly two instances. Ventriculography is a safe procedure and indispensable to the diagnosis and localization of many tumours of the brain. Each patient must be treated individually and certain time-tried policies must be strictly observed. A preliminary ventriculogram may be of decided value in planning the optimum method of operative attack. He advocates that injections of air be complete, particularly in view of localizing tumours in and about the third ventricle, aqueduct of Sylvius and fourth ventricle. Wide variance in operative exposures makes accurate localization here a *sine qua non*.

G. E. LEARMONTH

Spasmodic Torticollis Treated by the Plastic Reduction of Motor Fibres of the Spinal Accessory Nerve. Masson, C. B.: *Ann. Surg.*, 1938, 107: 287.

In 1934 Dogliotti published the results of his operative treatment on the facial nerve for

relief of spasmodic movements of the facial muscles. He thought that if the facial nerves on the affected side were severed, the central portion carefully split in half, and only one-half of the central end sutured to the entire peripheral end of the nerve, harmful nerve impulses could be reduced by at least 50 per cent. In so doing the nerve-muscle-threshold would be raised, and such impulses that did arise would be enough to supply tone to the facial muscles, and provide innervation for any of the former movements of expression, though not enough to cause spasmodic movements. This treatment has proved to be effective. Masson advises that this principle can be applied in conservative treatment for spasmodic torticollis. The usual radical operation, which consists of severing the first three anterior and posterior cervical roots, together with intradural section of one or both spinal accessory nerves, may rid the patient of troublesome spasmodic movements, but leaves him with quite a degree of weakness of movements of the head, neck and shoulder. Two cases are reported of the application of Dogliotti's principle in operation on the spinal accessory nerve. The nerve was exposed, sectioned and re-sutured, as above, at a point just before it enters the sternocleidomastoid muscle. In both cases a very satisfactory result was obtained.

FRANK TURNBULL

Functional Disabilities after Simple Fracture.

Gurd, F. B.: *Surg., Gyn. & Obst.*, 1938, 66: 489.

The author discusses the reasons for disability but more particularly in reference to acute bone atrophy. He does not give much space to anatomical abnormalities, non-union or fixation of tendons in the region of the fracture. Hysterical manifestations and the disability referred to as *sinistrose* are not included. There is a type of atrophy manifested clinically by the appearance, soon after injury, of swelling, marked pain, glazing of the skin, dusky red discoloration, with the joints stiff and their movements exceedingly painful. With absolute rest the pain soon disappears. On x-ray examination of the extremity distal to the fracture there will be found decalcification. This is at first patchy in distribution, but later becomes markedly rarefied generally. This is the chronic stage. Dr. Gurd agrees with other writers that the cause of this condition is probably to be found in the equation "less than normal function with normal blood supply—relative hyperæmia", then decalcification. He quotes J. E. Pritchard and his biopsy studies to show the embryonic form, osteoblastema, forming bone and tendon in the same lesion. With the occurrence of bone atrophy the attachments of ligamentous and tendinous structures will soften and even detach. The osteoblastema is capable of forming synovial cartilages, ligaments, tendons and bone and these structures are in fact inseparable in func-

tion and in the healing process. In the healing of atrophy in the upper extremity absolute rest is necessary. Prevention and treatment in the lower extremity may well be obtained by rest until complete disappearance of interstitial oedema and of pain with the later use of an unpadded walking cast. Hot baths increase the local metabolic processes and thus bring about relative decreased blood supply to the bone with increased calcification. Massage increases the muscular blood supply and so limits that readily available for the bone. Massage should never be used when it gives pain.

FRANK DORRANCE

Obstetrics and Gynecology

Hæmorrhagic Disease of the Newborn. Javert, C. T.: *Am. J. Obst. & Gyn.*, 1938, 35: 200.

The incidence of hæmorrhagic disease is 0.773 per cent in the hospital, and 0.304 per cent in the outdoor service. Parturitional factors are prolonged and severe labour, anæsthesia and analgesia and increased blood loss during the third stage of labour. Maternal debility, antepartum complications and age appear to have an influence. The intrauterine origin of hæmorrhagic disease is more than probable. Increased circulatory tension caused by the forces of labour may produce a separation of the capillary endothelial cells or actual rhexis of smaller blood vessels, thereby producing multiple hæmorrhagic lesions in the various organs. The multiplicity of the lesions suggests that the condition is a generalized systemic process.

One-third of the patients began to bleed during the first 24 hours of life, only 2 began to bleed after the first week. Bleeding precipitated by vascular trauma probably continues when the clotting or bleeding mechanism is abnormal. The fetal factors were immaturity and prematurity, anoxemia and prolongation of the bleeding time. The use of the mother as a blood donor is open to criticism. Rest of the bleeding organs, sedation and the administration of intramuscular blood are important. Transfusion is indicated when these measures fail, and in the presence of anæmia. Two and one-half per cent of 439 neonatal deaths were due to hæmorrhagic disease. The fetal vessels of the placenta offer an excellent opportunity of studying the fetal blood at the time of delivery. The same factors which cause excessive bleeding in the mothers probably predispose the infants to abnormal bleeding.

ROSS MITCHELL

The Significance of the Weakly Positive Ascheim-Zondek Test. Tenney, B. and Parker, F.: *New Eng. J. Med.*, 1938, 218: 561.

Reports on the Ascheim-Zondek tests for pregnancy in the Boston City Hospital are grouped as positive, weakly positive, and negative. In the definitely positive and negative tests there is no doubt about the interpretation. In the weakly positive cases there is often confusion.

The authors have followed 60 cases in which the report was weakly positive.

The pregnancy-urine prolactin is thought to be of placental origin, although it is so similar to the luteinizing hormone of the pituitary that its separate entity is not a certainty. It is this prolactin that gives the positive Ascheim-Zondek test. In the first two or three weeks following conception, injection of urine gives only a follicle-stimulating effect in immature rats. Following this early phase, enough pregnancy prolactin is present in the urine to produce definite corpora lutea in the immature rat. There is an intermediate stage where there is luteinization of the follicle cells without the formation of a distinct corpus luteum. This is the weakly positive test.

In a woman with a twenty-eight day cycle the Ascheim-Zondek test, made six weeks from her last regular period, should be definitely positive in a normal pregnancy. No patient with a weakly positive test had a normal pregnancy. This is of value in the treatment of threatened miscarriage. Such cases are apt to occur in the second and third months of pregnancy. A positive test at this time gives a good prognosis, while a weakly positive test gives a practically hopeless one. A weakly positive test is the first probability that one is dealing with a blighted ovum or an unhealthy pregnancy which will terminate in a miscarriage. A test is of prognostic value in a pregnant patient with staining in the second or third month.

In 12 of the 60 cases there was a tubal pregnancy; in 5 cases the fetus was dead; in the 4 non-pregnant patients 2 had hyperplasia of the endometrium and 2 had tubo-ovarian abscess. These are difficult to explain. Oestrogenic hormones are the essential cause of endometrial hyperplasia. This may be the result of an excess of the follicle-stimulating hormone of the pituitary. In the case of the tubo-ovarian masses where the ovary had been destroyed there may have been some castration effect on the pituitary. There was one case of hydatid mole. While an extremely high hormone content of the urine is present in well-advanced cases of hydatid mole and chorionepithelioma it is not present in the early stages.

After the first few weeks of pregnancy a weakly positive Ascheim-Zondek test indicates some abnormality. A weakly positive Ascheim-Zondek test may be of as much value as a positive or negative one.

LILLIAN A. CHASE

Urology

Urinary Tract Disturbances Referable to Cervicitis. Nelson, O. A.: *J. Urol.*, 1938, 39: 361.

During the last two years several papers have appeared which deal with infection of the cervix in relation to diseases and symptoms of the urinary tract. Experimental and clinical find-

ings justify the conclusions that cervical infection often does extend to the urinary tract. The tri-symptom complex which frequently presents itself is frequency of urination, backache, and leukorrhœa. The common finding on cystoscopic examination is trigonitis, with granular urethritis, and stenosis at the urethro-vesical junction. Other complications may arise, for example, upper urinary tract infection, and urinary lithiasis.

Infection in the deep portion of the cervix will at times not be discernible on either inspection or palpation. With the object in view of stopping the extension of the infection from the cervix to the urinary tract cauterization will usually fail to bring about the desired results. The author advises the Sturmdorf type of operation which, in the majority of instances, has brought about the relief desired. J. V. BERRY

Clinical Analysis of Therapeutic Measures in the Management of Pyogenic Prostatitis.

O'Connor, V. J.: *J. Urol.*, 1938, 39: 156.

From a critical survey of the measures used in the treatment of pyogenic prostatitis one must decide that there is no standard treatment which can be applied with equal effect in all instances. The author points out from a series of experiments with dogs, that over-frequent and too vigorous massage of the prostate gland results in rupture of the alveolar wall and in scattered cyst formations. O'Connor demonstrated further that, by massage, the gland could be traumatized to the extent that a marked round-cell infiltration resulted. The conclusion at which he arrives was that intelligent application of prostatic massage will be a benefit to most patients, but if carried out too frequently or for unduly prolonged periods there may be unfavourable reactions. A recognition, and elimination if possible, of the systemic focus seems the most important single consideration.

Treatment of the prostate itself should be primarily directed toward the relief of symptoms and, secondly, to the removal of persistent glandular infection. That chemotherapy may aid us in certain instances of pyogenic infection has been demonstrated repeatedly, the two most important agents being mandelic acid and sulfonamide. J. V. BERRY

Neurology and Psychiatry

Intraspinal Tumours in Infancy and Childhood.

Ingraham, F. D.: *Am. J. Surg.*, 1938, 39: 342.

In any infant or child presenting symptoms or signs referable to early pressure on the spinal cord, the possible presence of a tumour should be suspected. The history may be helpful, but objective observation must be chiefly relied upon. A complete neurological examination should be done, including not only observation of motor activity, reflexes, etc. but a sensory examination. This latter can be done with

patience even in a young and irritable infant. Cerebrospinal studies are valuable. Ingraham reports 16 cases in patients ranging from ten weeks to eleven years. Weakness of some sort was the presenting sign in 11 and pain in only five. The early diagnosis that was most frequently made on these cases was anterior poliomyelitis. In retrospect, there was not a single case in the series in which diagnosis could not have been made at an earlier date. In the majority of these patients slightly earlier diagnosis would have made a great difference in the end-result. All of these patients were operated upon. A fair proportion with rapidly growing malignant tumours had temporary relief from symptoms, and those with benign tumours (6) have been well since operation. FRANK TURNBULL

Blood Loss in Neurosurgical Operations.

White, J. C., Whitelaw, G. P., Sweet, W. H. and Hurwitt, E. S.: *Ann. Surg.*, 1938, 107: 287.

A large volume of blood is lost in major neurosurgical operations in contrast to the comparatively moderate amount lost during operations on the abdominal viscera, the thorax, and the extremities. In the course of extensive intracranial operations or laminectomy for tumour this hæmorrhage averages from 500 to 1,500 c.c. In spite of excessive bleeding, neurosurgical patients rarely go into shock if less than 1,200 c.c. of blood is lost, unless the hæmorrhage is rapid, or damage is done to the centres which control circulation and respiration. These patients tolerate long operations well and consequently allow a meticulous technique of hæmostasis. Ether or nitrous oxide as anæsthetics cause excessive bleeding. Infiltration of novocain-epinephrine solution into the scalp, supplemented by basal narcosis with avertin, is preferable. Replacement of blood lost during any extensive craniotomy is best carried out by a constant infusion of 5 per cent glucose in normal saline. One thousand to 1,500 c.c. administered in this way will take care of a gradual loss of a litre of blood. After a sudden brisk hæmorrhage, or failure of the organism to compensate for an excessive loss of blood, the infusion apparatus is available for the transfusion of citrated blood. Ordinarily, a single transfusion of 500 c.c. is sufficient after a hæmorrhage of from 1,200 to 1,500 c.c. FRANK TURNBULL

Therapeutics

Immediate Surgery in Acute Cholecystitis.

Clute, H. M. and Lembright, J. F.: *New Eng. J. Med.*, 1938, 218: 72.

Surgical opinion is gradually shifting toward immediate operative treatment of acute cholecystitis. "Acute cholecystitis" implies an infection of the gall-bladder. This is misleading. Most pathologists now agree that obstruction of the cystic duct is the primary factor and infection is almost always a secondary phenomenon.

In the authors' experience a stone was impacted in the cystic duct in 28 of 29 cases. Obstruction may also be caused by œdema. The development of œdema, necrosis, gangrene or perforation in the wall of the gall-bladder is therefore immediately dependent upon the extent to which the blood supply of the gall-bladder is involved by the swelling around the cystic duct. Bacteriological studies agree that infection of the gall-bladder is probably not the primary etiological factor.

In many respects the clinical picture of the early case of acute cholecystitis is identical with that of any early case of an ovarian cyst with a twisted pedicle, and the course after operation in each case is much the same. Obstruction is first in the course of events in acute cholecystitis, and is prerequisite to infection. Immediate removal of the obstructed viscus before infection has occurred is the procedure of choice. In many cases, however, there is a delay of several days before the surgeon is consulted, and it is often impossible to decide if infection has been superimposed on obstruction.

In theory it is best to operate on most cases within 48 hours of onset, in practice there is seldom an opportunity to do so. In 12 of 29 cases operation was performed 4 days or less from the time of onset. In these cases convalescence was easy and comfortable. These cases did not react after operation in any way like cases of abdominal infection. In 16 cases operation was performed 5 to 15 days after the acute attack. All these patients recovered, but several had a stormy convalescence; some had serious post-operative complications. The delayed operation is infinitely harder than the early one. Five patients had stone in the common duct. Only one of the stone cases showed jaundice; 4 other patients had jaundice but no stones in the common duct. Œdema about the junction of the cystic and common ducts was repeatedly noted.

The pathology of late cases of acute cholecystitis may be most deceptive; there is a very high percentage of error in correct diagnosis, particularly in the later stages. In late cases the authors observe the patient for hours or days while giving him fluids and glucose. If there is evidence of spreading infection, as suggested by a rising white-blood-cell count, a rising fever and heightening pulse, the authors favour immediate drainage of the gall-bladder. If the infection seems to be subsiding, delay and later operation is done.

LILLIAN A. CHASE

Immediate or Delayed Treatment of Acute Cholecystitis. Liver Shock and Death. Cave, H. W.: *Surg., Gyn. & Obst.*, 1938, 66: 308.

In acute inflammatory disease of the gall-bladder care in judging the individual cases is of utmost importance if operative mortality and post-operative complications are to be kept at a minimum. The "immediate" group include

such surgeons as A. J. Walton, Graham, Leriche and Cotte; Finney and others are in favour of treating the acutely inflamed gall-bladder in much the same manner as the acute appendix. The author has reviewed these writers and finds they should really be considered "early" operators. That is, the majority consider 48 hours to 7 days may be utilized in preparing the patient, although gangrene and rupture may be considered as "immediate" indications, but proper preparation is as essential. Practically 90 per cent of patients acutely ill with acute cholecystitis will find the acute stage to subside. It is well to wait 24 to 36 hours to observe the temperature, pulse, and white blood count. Liver shock and death may be of 3 types: (1) in patients with chronic cholecystitis with jaundice, failure to regain consciousness with increased temperature and pulse rate and death in 36 hours; (2) in obstructive jaundice with choledochostomy satisfactory progress for 3 to 4 days become delirious and comatose; (3) diseased pancreas and bile ducts without jaundice, after satisfactory progress for a few days apparent circulatory failure occurs. These might be prevented by more thorough blood chemistry examinations and particularly the estimation of xanthoprotein, indican and cholesterol esters, the sedimentation rate. Urea nitrogen variation warrants liberal use of water and above all assurance of glycogen storage. Blood transfusions after prolonged operating time or blood loss should be done.

FRANK DORRANCE

Pathology and Experimental Medicine

Identical Cancers in Identical Twins. Phillips, R. B., *Proc. of the Staff Meetings, Mayo Clinic*, 1938, 13: 209.

Twin sisters of the identical type both developed bilateral mammary carcinoma. The tumour was thought to be primary in each breast in each sister, in all probability. The first twin developed a tumour in the right breast in 1927, the second twin a tumour in the right breast in 1930. The first twin developed a tumour in the left breast less than a year after she had developed one in the right. The second twin developed her tumour in the left breast two years after she had shown the first tumour. All four tumours were carcinomata. Ten years after her first breast tumour, the first twin developed bilateral ovarian carcinoma. The question is brought up as to the treatment which should be given the second twin. Will she develop ovarian cancer; should she be given prophylactic deep roentgen therapy; should the ovaries be removed to prevent the onset of cancer?

The family history was that a paternal aunt of the twins had died of cancer of the breast at 45. Their elder sister had a "lump" removed from her breast in 1927 and is now alive and

well at 55. The father and mother died at 75 and 80, respectively, presumably without cancer. This case adds one more interesting example to the list of tumours in twins. It is of peculiar interest because of the development of bilateral primary tumours of the breast in both twins. We will look forward to a completion of the story that the second twin develops ovarian cancer, or that she lives many years without it. The record will be equally valuable in either case.

MADGE THURLOW MACELIN

Hygiene and Public Health

The Contribution of Industry to Medicine.

Bashford, H. H., *Proc. Roy. Soc. Med.*, 1938, 31: 185.

Dr. Bashford is the chief medical officer of the British Post Office and in this capacity he supervises the health of some 260,000 employees. The age of these employees ranges from 14 to 60, and many occupational groups are included. The medical service of the post office has been in operation for three-quarters of a century, and its records lend themselves in a rather unique fashion to research into the significance of various medical or surgical conditions. The author records briefly some of the investigations that have been made.

The experience with pulmonary tuberculosis has not been good. Only 50 per cent of new cases are able to return to work, and nearly half of these are compelled to give up on account of recurrence or other conditions.

In the case of gastric and duodenal ulcer the experience is also unsatisfactory. Thirty-one per cent of ulcer cases, confirmed by x-ray, incur a month's sick leave or more every year, another 27 per cent from two to four weeks' sick leave.

On the other hand experience has enabled the post office to relax some of their restrictions on the employment of adolescents with albuminuria. About 5 per cent of young boys and 16 per cent of girls show albuminuria at the time of the employment examination. The experience of those who have actually been employed has been very favourable. So much so that in the opinion of Dr. Bashford albuminuria *per se* in young persons is of no material importance.

An interesting observation which is in line with certain observations elsewhere is to the effect that the present generation is actually heavier and taller than the past. Actually the boys in the post office group average 16 pounds more in weight and 1½ inches more in height than the boys from the same sort of environment 25 years ago.

The quite extensive experience of the post office with anti-eatarrhal vaccine was not impressive and led to the opinion that the procedure was not justified by the results secured. A somewhat similar conclusion was reached

after a rather limited trial of vocational guidance.

With regard to quarantine of contacts with cases of communicable disease the earlier restrictions have been greatly relaxed, with a resultant saving of thousands of days of lost time and no evidence of an increase in secondary cases among the staff. Data are given that in the age group concerned 1 out of every 251 contacts with scarlet fever contract the disease, 1 out of every 670 measles contacts and 1 out of every 274 diphtheria contacts. This would appear to be altogether too small a percentage of secondary cases to warrant quarantine of all contacts.

FRANK G. PEDLEY

The Influence of Moderate Carbon Monoxide Poisoning upon the Ability to Drive Automobiles. Forbes, W. H. *et al.*, *J. Indust. Hyg. & Toxicol.*, 1937, 19: 598.

In eleven experiments upon 8 normal men it was found that their performances in simple tests of reaction times, binocular vision, coordination of the hand and eye, etc., were unaffected by breathing carbon monoxide until their blood was 30 per cent or more saturated. At 45 per cent saturation their performance was only slightly impaired. Subjectively, they felt normal at 30 per cent saturation or less, but at 45 per cent both appeared and felt unequal to driving a car because unable to think of many things at once. The pulse, respiration and blood sugar were unchanged up to 30 per cent saturation.

FRANK G. PEDLEY

Obituaries

Dr. William Edmund Anderson, of Lake Alma, Sask., died on May 13th in his 67th year.

Although in ill health for a number of years, Dr. Anderson practised his profession until his recent serious illness. A native of Orillia, Ont., he received his higher education in the Ontario College of Pharmacy, also in California, South Bend, Indiana, and Queen's University (1910), coming to Saskatchewan in 1919.

He was a capable artist and a lover of good music.

Dr. E. Douglas Ayles, of Montreal, died on May 14, 1938, in his 67th year, following an illness lasting eight years. He was born at Aylmer, Que., the son of the late John Ayles, M.D., LL.B., and received his medical training at McGill University from which he graduated in 1893. He was an intern for two years at the Montreal General Hospital and then opened his practice at Hochelaga. He retired eight years ago when his health failed.

Dr. James Lyons Biggar, of Toronto, died on June 2, 1938, after an illness of several months. He was born in Toronto and had just passed his sixtieth birthday. He was a graduate of the University of Toronto (1903).

Dr. Biggar served in the South African and the Great War, and prior to 1914 practised medicine at Toronto, Tillsonburg, Ont., Edmonton, Alta., and

Victoria, B.C. He had been head of the Canadian Red Cross since May, 1926. In the early years of his career he was house surgeon at the Toronto Hospital for Sick Children and on his return from service overseas in 1910 he became assistant medical adviser to the Board of Pensions at Ottawa. He served as a private and then as a corporal in the South African War, and in the Great War was an officer in the Canadian Army Medical Corps, with the rank of Lieutenant-Colonel.

Dr. Overton William Bradley, of Montreal, died on May 29, 1938, in his sixty-third year. He had practised in the district of Point St. Charles for thirty-five years.

Dr. Harry Howard Galloway died at his home in Alameda, Sask., May 4th, after several months' illness. The son of William and Mary Jane Galloway, of Oxbow, Sask., he was born on November 6, 1879, in Bethany, Ont. He came with his parents in early years to reside in the Oxbow district, and after attending high school, graduated in medicine from Trinity University, Toronto (1906). In 1907 he located in practice in Alameda, where he had resided since. He was widely known over the entire southern portion of the province, and took an active interest in all community activities, a keen student of political economy. He was for long District Health Officer.

Dr. George L. Hume, of Sherbrooke, Que., died suddenly on May 31, 1938, aged sixty-nine. He had practised in Sherbrooke for thirty-three years, and was a graduate of McGill University (1898).

Dr. Richard John Ledwell, of Charlottetown, P.E.I., died on May 31, 1938, aged sixty-three. He was born in Charlottetown in 1875, son of Mrs. Catherine Ledwell and the late Captain J. H. Ledwell. He attended St. Dunstan's University and Prince of Wales College. He entered Tuft's College, Boston, for the study of medicine and graduated from this institution in 1901, when he entered the Boston City Hospital. Later he entered the Boston Emergency Hospital, before returning to Charlottetown where he practised for 33 years.

Besides his widow, he is survived by one son, John S. Ledwell, M.D., C.M., of Charlottetown, and his mother, Mrs. Katherine Ledwell.

Dr. Fernandoy Duharte Llorens, of Sheet Harbour, N.S., died after a brief illness, on June 8, 1938. He was thirty-eight years of age. Dr. Llorens was a native of Cuba. He graduated in Arts from the University of North Carolina and, after teaching school for a short time in Georgia, came to Dalhousie, taking his medical degree in 1931. He went into practice on Nova Scotia's eastern shore, settling in Sheet Harbour in 1935, where he soon established a reputation among his colleagues as an expert diagnostician. He is survived by his widow, the former Mildred Caldwell, of Falmouth, his son, Thomas, aged eight, and daughter, Dolores, aged five.

Dr. James Moore, of Trowbridge, Ont., died on April 10, 1938. He was a graduate of the Medical Faculty of Trinity University (1900).

DR. GEORGE PIRIE: AN APPRECIATION

Dr. Pirie was a great clinician and while he had every confidence in the modern laboratory methods of diagnosis he felt that these methods should be used in proving the diagnosis, and that the findings were only of value where they correlated the history and physical findings of the trained clinician. He believed there was less chance of error with a careful and thorough physical examination than in a diagnosis made, partly at least, by laboratory procedures, and

often completed by individuals with no intimate contact with the patient.

He was particularly interested in the abnormal heart and it was in these cases where he demonstrated his ability to diagnose and outline a prognosis frequently earlier than and more accurate than those arrived at through laboratory methods. He worked out a graphic interpretation of heart sounds and their relation to each other, giving the clinician a means of early diagnosis of heart involvement. In addition he was convinced that the prognosis in pneumonia could best be made by attention to the heart sounds, particularly the second aortic, regardless of the amount of lung involvement. In this he was almost invariably correct.

Dr. Pirie's greatest forte was his ability to teach, and though his footsteps will no longer be heard in the wards of the Children's Hospital, his teachings, not only to students but to house physicians, visiting physicians and fellow staff men as well, will aid the sick child both here and wherever our physicians travel. No matter how far forward methods of diagnosis other than clinical may advance, the good clinician, as exemplified by George Pirie, will still be the foundation of successful medicine and sound practice.*

ALAN BROWN

Dr. Alexander White Richardson, of Kingston, Ont., died on April 23, 1938, after a long illness. He had been a resident of Kingston since 1895.

For some years Dr. Richardson was minister of First Congregational Church, Kingston. While in that charge he entered the School of Medicine at Queen's University and graduated in 1899. He resigned his pastorate in 1902 and until his fatal illness practised medicine. He served as alderman for three years and was mayor of his city in 1916.

Dr. Hugh Ross, of New Glasgow, N.S., died at his home on May 31, 1938, in his seventy-first year. Born at Telford, Pictou County, Dr. Ross graduated from McGill University in 1894 and did post-graduate work in New York and London. He practised in Stellarton for seven years, then moved to Canso, where he was medical officer of the Commercial Cable Company at Hazel Hill for eighteen years. After further post-graduate work in London in 1922 he settled in New Glasgow. He was senior member of the staff of the Aberdeen Hospital.

Surviving him are his widow and three sons, Ian G. Ross, LL.B. and William Hugh, at home, and Donald at Washington.

Dr. John Garth Toombs, aged 39, of Moose Jaw, died on May 5th in Providence Hospital.

Dr. Toombs was born at Mount Stewart, P.E.I., in 1899, the son of Dr. and Mrs. J. D. Toombs. He received his primary education in Charlottetown and took his Arts course in Mount Allison College, Sackville, N.B. He graduated from Dalhousie University with his medical degree in 1927. Dr. Toombs was an intern in the Victoria General Hospital, Halifax, prior to coming to Moose Jaw. He took a post-graduate course in London, England, in 1935, and again in Chicago in 1937. Dr. Toombs came to Moose Jaw in 1928 and joined with Dr. G. S. Goodwin in practice.

He enlisted in the 105th overseas battalion in 1915, went overseas in 1916, transferred to the signal corps, and was attached to the Second Canadian Machine Gun Corps as a signaller. He received his commission as a medical officer in the 10th Field Ambulance in 1929, and two years later was promoted captain. In 1933 he was transferred as medical officer to the King's Own Rifles, which appointment he held to his death.

* Biographical and other details about Dr. Pirie have appeared in the *Journal*, 1938, 38: 619, and are, therefore not repeated here.—[Ed.]

Dr. Toombs was one of the medical officers of the St. John Ambulance Association, an honorary member of the Order of St. John of Jerusalem, and an enthusiastic exponent of the teaching of "first aid". He was a member of the Moose Jaw Military Service Institute, the Elks lodge and the Moose lodge.

Dr. Toombs married Doris Leard, daughter of the late Dr. and Mrs. A. W. Leard, in 1929, and is survived by his widow; one son, his mother, one brother, and three sisters. He was buried with full military honours.

Dr. John Farrell Wood, of Manitou, Man., died on May 7th. He was born in St. Jean Baptiste, Man., but was raised on his father's farm in the Miami district. He graduated in Medicine in 1914 from the Manitoba Medical College and in the fall of that year enlisted for active service with the R.A.M.C. He served in the war areas of Gallipoli, Egypt, Mesopotamia, and France, and received decorations for his services. At the time of his death he held the position of Medical Officer of the Manitoba Mounted Rifles, holding the rank of Major. On his return from overseas Dr. Wood entered into partnership at Manitou with Dr. I. H. Davidson, and later took over the entire practice. He was the Medical Officer of the Municipality of Pembina and of Manitou, took an interest in the sports' organizations of the town and was an ardent golfer. He is survived by his widow and one daughter.

News Items

Alberta

Officers of the Canadian Medical Association, Alberta Division, and others have been making a tour of various districts in the province. The following program was carried out: Dr. C. R. Bunn, President-elect, gave addresses on "Aims and objects of district meetings; Representatives on the Nominating Committee and Board of Representatives." He also discussed medical economics, federation with the Canadian Medical Association, and urged all members to attend the annual meeting of the Association next September. Dr. G. R. Johnson, Honorary Secretary of the Canadian Medical Association, Alberta Division, and Registrar of the College of Physicians and Surgeons of Alberta, discussed the workings of the College and the importance of the Association and the College working in the closest cooperation.

Dr. W. H. McGuffin, Chairman of the Provincial Cancer Committee, stressed the importance of the new Cancer Control Organization, and with great detail showed how all of the citizens could and should assist this great forward movement for the benefit of mankind. At each place visited he met committees of members of our profession as well as laymen.

Dr. W. A. Lincoln, F.R.C.S.(Eng.), made a strong plea for the family physician and reliance on clinical knowledge rather than showing too great dependence on the laboratory and mechanical means of diagnosis. He also gave a paper on acute abdominal lesions which was much appreciated.

The College of Physicians and Surgeons of Alberta has made a survey of a portion of the province which suffered from drouth, and found many municipalities without physicians where formerly they had them. In the north-eastern area there were twenty-five fewer physicians than formerly. The following facts were noted.

That tax assessments were greater than the requirements, by a large amount, to provide for those who did not pay; that money could be found for seed,

feed for stock, and oil for tractors, but for people who were ill the federal authorities gave no assistance. The hospitals were advised that no accounts would be guaranteed for services to the people presently on relief or to indigents, unless they continued to be on relief after the present crop was harvested. That physicians in the worst dried-out areas received the least consideration. That in most of these dried-out districts the population had not decreased measurably but no medical services were to be had.

The Annual Refresher Course presented by the University of Alberta was held in May as usual, but with a larger attendance than formerly. Over fifty physicians attended, though some were able to remain a day only. The efforts of the Medical Staff of the University are greatly appreciated by the Provincial Medical Association as a whole, as well as by those who were privileged to be present.

The Workmen's Compensation Board is endeavouring to change the form of report (first) of the injured workmen, and are hoping that the new form will prevent errors in names, delays in accepting responsibility, increase the promptness of accepted claims being paid, and reduce the work of the office staff. If it does half what is thought it might do, from the Board's standpoint, without transferring the burden to the doctor, it will be well worth while.

G. E. LEARMONTH

British Columbia

An anonymous donor, who is a Vancouver citizen, has made a cash gift of \$50,000 to the British Columbia Cancer Foundation. This donation is to be used in connection with processing radium at present in the hands of the Foundation and to open a temporary clinic in one of the buildings on the property of the Vancouver General Hospital.

The City Council of Vancouver has sold to the provincial government the property upon which the Vancouver Institute for Diseases of the Chest has been built. It had only recently been discovered that this property was owned by the City of Vancouver. The property was sold for \$1.00.

The negotiations with Commissioner Fraser, of Burnaby, a municipality adjoining Vancouver, regarding the membership of that municipality in the Metropolitan Health Board are progressing satisfactorily, and it is anticipated will be completed shortly.

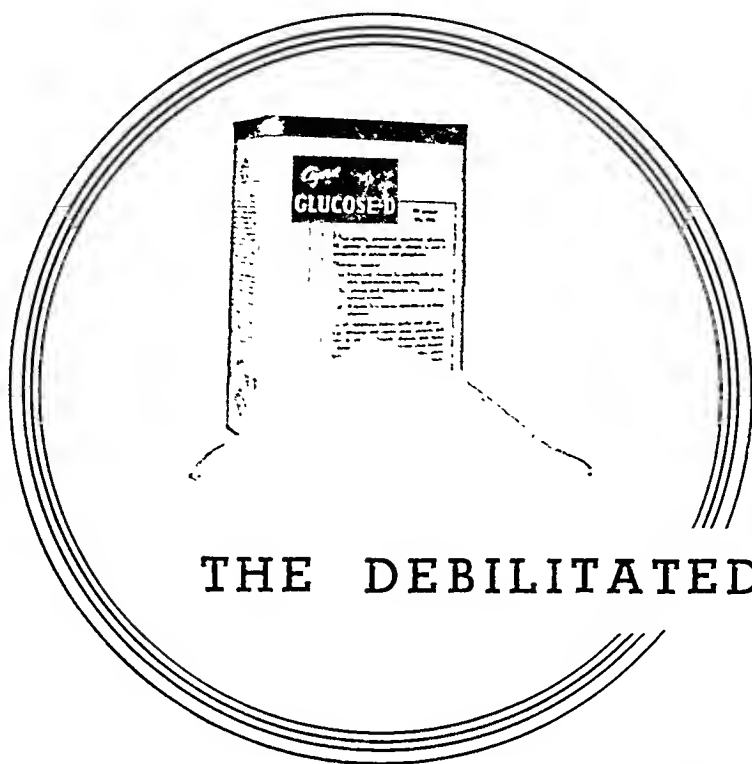
D. E. H. CLEVELAND

Manitoba

The forms in connection with the Maternity Survey in the Province of Manitoba have been sent out. The survey started on May 1, 1938, and is made possible by the cooperation of the Rockefeller Foundation, the Dominion Department of Health, and the Manitoba Department of Health and Public Welfare. A fee will be granted to the doctors who file completed records. It is expected that the survey will not only yield valuable statistical information but will assist in raising the standard of obstetrical care in the province.

It is announced that the Sisters of Charity of St. Hyacinthe, Que., will build a hospital at Flin Flon, where the Hudson's Bay Mining & Smelting Company's mines are situated. It is this Order who built St. Anthony's Hospital at The Pas.

Dr. L. A. Sigurdson gave an interesting talk on Iceland's medical history at the meeting of the Medical Club in the Medical Arts Club Rooms on April 28th. A number of slides illustrative of the island's



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CANADA

scenery and culture were shown. Dr. Sigurdson stated that there were more Icelanders in Winnipeg than in any other centre outside Reykjavik, the capital of Iceland. Dr. S. J. Johannesson was present at the meeting, and spoke of the thirty-one years he spent in Iceland before coming to Canada. Dr. Sigurdson announced that on the evening of Monday, April 26th four hundred Icelandic citizens had met at dinner to honour Dr. Johannesson on the occasion of his seventieth birthday and as a mark of appreciation of his Icelandic poetry.

Dr. Omar G. Hague, former Radiologist at St. Boniface Hospital, on June 1st began action in the Court of King's Bench to compel the Cancer Relief and Research Institute to place him on the list of physicians entitled to receive radium. In his claim he states that up to January 4, 1938, he was entitled to obtain radium and radium emanations from the Institute and that on that date he was informed he was no longer so entitled. Dr. Hague asks for a mandamus and \$5,000.00 and costs.

The Cancer Relief and Research Committee was organized several years ago to control the administration of radium owned by the province. It has eighteen directors, three each being nominated by the University of Manitoba, the Union of Manitoba Municipalities, the Provincial Government, the Manitoba Medical Association, and the Winnipeg Medical Society, with three members at large. The present chairman is Mr. R. G. Persse.

On June 1st a four-roomed structure, added to the King Edward Hospital and built at a cost of \$13,600.00, was formally presented to the City of Winnipeg by Sister Edith Patricia, daughter of the donor, the late Martin T. McKittrick. The addition will be used for the examination of tuberculous suspects.

The Sanatorium Board of Manitoba has determined that a memorial to the late Superintendent of Manitoba Sanatorium, Dr. D. A. Stewart, will be erected on the grounds of the Sanatorium at Ninette. A committee is arranging the details.

ROSS MITCHELL

New Brunswick

The Imperial Order, Daughters of the Empire, of Saint John, have sponsored the well-baby clinics in the city. These clinics will be held in the Health Centre under the supervision of Dr. W. F. Porter and Dr. Stanley Bridges.

The new intern staff at the Saint John General Hospital have assumed their duties. The larger number are final year students from Dalhousie University. In the last few years this type of house physician has proved of eminent value in the smooth working of the clinical departments of the hospital.

The Provincial Government has recently authorized an expenditure of considerable funds for alterations and extensions at the Provincial Hospital. This will allow for an increase in accommodation of approximately 150 patients in this institution.

Plans for the extensions to room accommodation and new galleries at the St. John Tuberculosis Hospital are being advanced satisfactorily.

Dr. Gordon Corbett, of Saint John, has returned after a four months' intensive course in paediatrics, during which time he studied at clinics in New York, Philadelphia, St. Louis and Montreal.

Dr. Kenneth Sullivan is at present doing post-graduate work at Baltimore.

Dr. J. P. McInerney is substituting for Dr. J. M. Barry this year as an examiner in Medicine at Halifax for the Dominion Medical Council.

Dr. Charles McMillan, M.O.H. for the Southern District of New Brunswick is being congratulated on the success of the Provincial Musical Festival just completed. Dr. McMillan has been President of the Provincial Musical Festival Organization for the past two years.

A group of medical militia officers went to Boston in the first week in June, as specially invited guests, to attend the 300th anniversary of the formation of the Ancient Honorable Artillery Company of Massachusetts. Included in this group were Lieut.-Col. V. D. Davidson, Lieut.-Col. R. A. Hughes, Lieut.-Col. C. M. Pratt, and Lieut.-Col. D. C. Malcolm.

Dr. J. M. Barry, Registrar of the College of Physicians and Surgeons of New Brunswick has been confined to hospital and his home during the last month suffering from a carbuncle.

Dr. W. F. Porter, of Saint John, read a paper on "Intracranial hemorrhage in the new-born", at the meeting of the Washington County Medical Society at Eastport, Me., on May 26th.

Dr. W. W. White, of Saint John, has been confined to his home by illness for many weeks.

A. STANLEY KIRKLAND

Nova Scotia

Wednesday afternoons and Sundays off will be the rule for the Truro profession during the summer months, according to regulations they have announced to the public. A relay of three doctors will be on duty during the closing periods and all work will be referred to them. Similar plans have been used in some of the mining towns where most of the patients are on the check-off system, but the Truro move is, so far as we know, a pioneer effort among the ordinary communities in Nova Scotia.

Dr. Allan R. Morton (Dalhousie '25) has been appointed City Health Officer for Halifax, succeeding Dr. W. Bruce Almon who retired after many years of service. Thoroughly trained in psychiatry and in chest work as well as in general medicine Dr. Morton is well fitted to deal with the problems most pertinent in the public health of Halifax.

United Mine Workers in a sub-district convention at Glace Bay expressed disapproval of the present check-off plan for doctor's fees. The miner pays forty cents per week to his doctor, seventy cents in all for hospital and medical care. Such an amount, it was felt, should be sufficient to cover all expenses, but, under the present system, the advice and care of specialists in Halifax, Montreal and other centres, when necessary, calls for extra expenditure. Most popular suggestion and plan to be followed for further investigation is that a central clinic be established in conjunction with the two Glace Bay hospitals, employing a full-time, salaried staff trained to administer any type of service required.

Dr. W. J. Dyer (Dalhousie '36) of the medical staff of the Kentville Sanatorium has resigned his post to take charge for the next few weeks of the public health clinics in Lunenburg, Queens and Yarmouth counties. Later, Dr. Dyer will take up post-graduate work in general and chest surgery at the Royal Victoria Hospital.

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B. coli contamination of the Dartmouth water supply has brought warnings from Dr. Payzant, town health officer, but the source of the contamination after some weeks still remains undiscovered.

A full-time health officer for Halifax instead of a part-time appointment was recommended to the City Council by the local branch of the Nova Scotia Medical Society. This is in line with recommendations the society has been making for some years but the City Council did not see fit to act upon them at present.

Dr. Joseph Hayes (Penn., '88) recently celebrated the fiftieth anniversary of his graduation.

ARTHUR L. MURPHY

Saskatchewan

All speakers at the meeting of the College of Physicians and Surgeons of Saskatchewan at Waskesiu will be from outside the province to enable the Saskatchewan men to have their time free. The following have agreed to contribute to the scientific program: Drs. Alexander Gibson, Winnipeg; J. D. McQueen, Winnipeg; M. R. Levey, Edmonton, and D. S. McNab, Calgary.

A feature of the business session will be the presentation for approval of the application to become a division of the Canadian Medical Association. Application has already been made, provisional to its acceptance by the meeting of the College of Physicians and Surgeons of Saskatchewan at Waskesiu.

Picnics and golf tournaments have been arranged so that there will be plenty of opportunity for the outdoor life.

LILLIAN A. CHASE

United States

A Course in Medical History.—For the first time, certainly in the United States of America, and possibly in the world, a graduate course has been devoted to the history of medicine. That stimulating scholar and philosopher, Henry Ernst Sigerist, Welch Professor of the History of Medicine at the Johns Hopkins University and Director of its Institute, through a carefully planned program brought together at a Baltimore during the week of April 18 to 23 a large and enthusiastic group of men and women from the United States and from Canada, among whom were a number of distinguished historians. The President of the University, Dr. Isaiah Bowman, opened the proceedings. The morning sessions were devoted to lectures and discussions and included such topics as principles of primitive medicine, Egyptian medical papyri, the Hippocratic problem, Paracelsus and the development of iatrochemistry, new contributions to the history of the circulation of the blood, and the social history of medicine in the nineteenth century. In the informal atmosphere of the afternoons' round-table seminars, attention was primarily focused on problems concerning teachers of medical history, such as the various approaches to its study, the interpretation of medical texts, the history of disease, and the choice of a subject for research. The more strenuously educational part of the course was skilfully mollified and at the same time enhanced by exhibits, visits to libraries and learned societies, cocktail parties, and dinners. The vast armamentarium of research and equipment which the Institute commands was made available to those desirous of learning for themselves how medical history may be pursued as an exact

scientific study and how it may also be temptingly and successfully introduced into medicine's daily work. Just as in international congresses, one of the more valuable aspects of this graduate week also was the opportunity it afforded of meeting kindred spirits and of discussing individual problems with Dr. Sigerist and his staff, who freely gave their undivided attention. The most original item on a crowded program was a musical evening in the Great Hall of the Welch Medical Library, which houses the Sargent Portrait of the Four Professors. Four string instruments and one soloist performed music which had not been heard for two or three centuries: a frottola on the syphilis of Marchese Francesco Gonzaga of Mantua (1517); dance music played in Southern Italy during the seventeenth century in the treatment of that astonishing disease tarantism; and hymn-like music in praise of St. Sebastian, patron saint against the plague (1702). Intended purely as an experiment, this graduate course was by common consent so helpful and so delightful that it will be repeated in future years and should become a recognized feature of medical education in America and possibly also in other countries.—*Brit. M. J.*, 1938, 1: 1163.

General

The Third International Goitre Conference is to convene in the City of Washington, District of Columbia, U.S.A., September 12 to 14, 1938.

Physicians and others in the United States and in other countries desirous of participating in the program are requested to submit titles at their earliest convenience. Since the time which it is possible to allocate on the program is obviously limited it will be necessary for the Program Committee to exercise its best judgment in the selection of speakers, and to insist without exception that the speakers conform to the time allocated.

Manuscripts of addresses, papers and discussions delivered or read at the meetings are to be published *in extenso* in the form of transactions. The official language of the Conference shall be English. Interpreters will be furnished for papers read in other languages. For further information concerning the Conference, communicate with the officers of the American Association for the Study of Goitre or the Chairman of the Program Committee, Dr. Allen Graham, 2020 East 93rd St., Cleveland, O., U.S.A.

Lectures on Nutrition.—Arrangements have been completed for addresses on Nutrition, under the auspices of the Association's Committee on Nutrition, to be given by Prof. L. H. Newburgh, of the Department of Internal Medicine, University of Michigan, in September, at Victoria, Vancouver, Calgary, Regina and Winnipeg. These addresses will be open to the general public, but Professor Newburgh will also take part in the scientific programs of the various provincial medical meetings which are held in that month in the West.

It is also announced that Sir Edward Mellanby, Director of the Medical Research Council of Great Britain, with Lady Mellanby, will visit Canada the last week in September and the first week in October. Sir Edward will give public addresses on Nutrition in Montreal, Ottawa, Kingston, Toronto and London.

Dr. Herbert S. Birkett (Montreal), Dr. Brown Kelly (Glasgow), Dr. D. R. Paterson (Cardiff), and Sir StClair Thomson have been elected Honorary Members of the Gesellschaft Deutscher Hals-, Nasen- und Ohrenärzte.

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Book Reviews

Modern Treatment in General Practice, a Yearbook of Diagnosis and Treatment for the General Practitioner. Edited by C. P. G. Wakely. Vol. 4, 440 pp. \$3.00. Macmillan, Co., Toronto, 1938.

For the fourth successive year we welcome these volumes from the *Medical Press and Circular*, which are finding a place in so many libraries. They consist of about 450 pages of articles contributed by specialists, and written with the needs of the general practitioner always uppermost. This latest contribution to the series not only has interesting chapters on medical and surgical conditions, most of them of everyday frequency, but it contains a new departure, "Pitfalls in Diagnosis", where such things as left iliac pain, diarrhoea, constipation, chronic cough in childhood, certain fractures, and lesions of the skin are discussed from the standpoint of diagnosis. The reader will appreciate this addition to an already valuable yearbook. The high lights in this volume are: Principles of treatment of non-specific inflammation of the skin, by Whitfield; Treatment of alcoholism, by Barham; Pain in the iliac fossa, by Sir John Fraser, and Dermatitis artefacta by Goldsmith.

Neuro-ophthalmology. R. L. Rea, B.Sc., M.D., M.Ch., F.R.C.S. 516 pp., illust. 42s. William Heinemann, London, 1938.

This work is designed as a liaison between the field of the ophthalmologist and that of the neurologist. It is not designed, avowedly, to be all-comprehensive, although it is hard to find much of importance that has been overlooked. The author hopes that his work may be of value to many of the younger ophthalmic surgeons who are attached to neurological clinics as well as to students of neurology. We think his hope is well founded. Indeed, there is much in the book that every medical man should know.

Opinions will differ, doubtless, as to what and how much should be admitted into a work of this character. Chapter I, entitled Equipment necessary for Examination of the Eye, is probably superfluous for the trained ophthalmologist and too detailed for the average neurologist. Possibly more might have been said about the ophthalmoscope and the mode of using it, as, nowadays, every medical man should be expert with it. In places the author is discursive and wanders into bypaths. Thus the discussion on the relationship between herpes and varicella, while interesting, seems hardly necessary, nor does the somewhat lengthy disquisition on the place of alcohol, while doubtless sound, seem to be in place. The action of the extraocular muscles is not so clearly described as might be, and more attention might have been given to Stutterheim's theory as to asthenoconvergence. On the other hand, many conditions are described which are not usually described in textbooks of ophthalmology. Chapters XV on The Ocular Manifestations of Head Injuries; XVI, on The Poisons which affect Vision; and XVII, on Headache and Amaurosis, seem to us worthy of special commendation. The neurologist possibly may find the account given of nervous diseases too sketchy, but, after all, the work does not purport to be a textbook of neurology. Particularly valuable are the tables giving the list of causes of various conditions. To compensate for any lack in the text the author has appended a bibliography to which the reader may turn for full details on any subject. The illustrations, many of which are in colour, are excellent. The work is well planned and well carried out. It is to be regretted that in a work of such high quality the English is not impeccable. For example, "data is" will not pass. Some errors in spelling have slipped by the proof reader. On page 488 "Hensen" should be "Hansen".

This is an outstanding book.

Poulsson's Textbook of Pharmacology and Therapeutics. S. Alstead, M.D. 2nd ed., 557 pp. \$7.50. Macmillan, Toronto, 1938.

For nearly a generation this work has been considered a standard textbook in northern Europe. Dr. Alstead has undertaken in this revised edition to bring it in line with the most recent British and American Pharmacopœias, to delete many remedies which have outlived their usefulness, and to add others whose value has yet to be proved.

In a book of 550 pages the author has covered the field of pharmacology in a manner most acceptable to the senior student and the practitioner. Only the main features are dwelt upon, and where there has been a difference of opinion among experimenters both sides of the argument are fairly stated. The direct application of the science to therapeutics is always kept in the foreground, for the great majority of the readers will be physicians.

The various preparations of drugs are discussed from a thoroughly scientific standpoint, and the old stock phrases of the last decade—"said to be useful in such a condition", "has been recommended for this disease", etc., have entirely disappeared. Although wisely conservative, the book includes such recent additions to our armamentarium as sulphamylamide, protamine zinc insulin, merbaphen and ergamine.

Essentials of Psychiatry. G. W. Henry, M.D. 3rd ed., 465 pp. \$5.00. University of Toronto Press, 1938.

The fact that three editions of this popular textbook have been necessary in twelve years speaks highly of its popularity among students and the profession. Psychiatry in the meantime has made great progress and now occupies a much more important place on the medical curriculum than it did when this work was first printed, so that the author feels the necessity of a complete revision. This, however, has followed the outline he adopted in the beginning—to present the main facts of the subject in language unclouded by a complicated nomenclature, and at the same time to deal adequately with personality disorders, which each year seem to play a more important part in the practice of medicine. This work has always been looked upon as an excellent introduction to the field of psychiatry, and the third edition makes it even more valuable.

Chiropody, Theory and Practice. F. Charlesworth, F.B.A.Ch. 2nd ed., 204 pp., illust. 15s. Actine Press, London, 1938.

This book is essentially for the chiropodist and it has little value for the medical man. The author's aim is to make the chiropodist someone who has much more than a superficial knowledge of the subject and the part of the body with which he deals. With this end in view the book is divided into two parts. The first eleven chapters deal with osteology, connective tissue, the normal arrangement of knee, ankle and foot, the anatomy of the muscles, arterial and nervous supply of the leg, ankle and foot. The remainder of this part of the book deals briefly with bacteriology, sterilization and hygiene in surgery. The final part deals with materia medica of the drugs used in the practice of chiropody. This part of the book is clear and puts forward the essential parts without too much intricate detail. The second part of the book, composed of eleven short chapters, deals with the treatment of pathological conditions which are usually met with by the chiropodist. The author realizes his limitations and quite freely advises the patient to consult a surgeon when he feels the condition is beyond the scope of his training.

While one may disagree about the usefulness of such a book yet the author really has tried to improve the status of chiropodists by giving them a more complete knowledge of the anatomy and physiology of their subject and at the same time he points out the limitations in procedures especially operative and manipulative.

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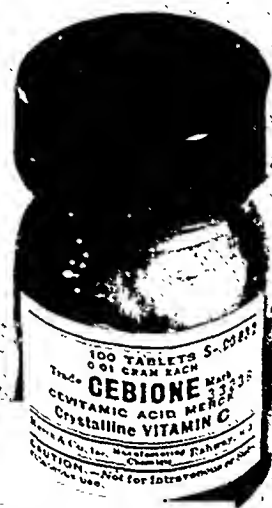
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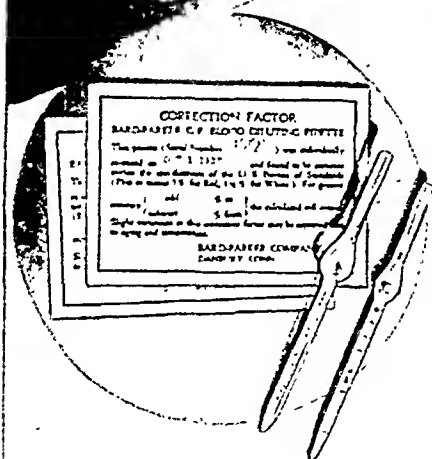
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* Swartz and Reilly "Diagnosis and Treatment of Skin Diseases", p. 66-67.

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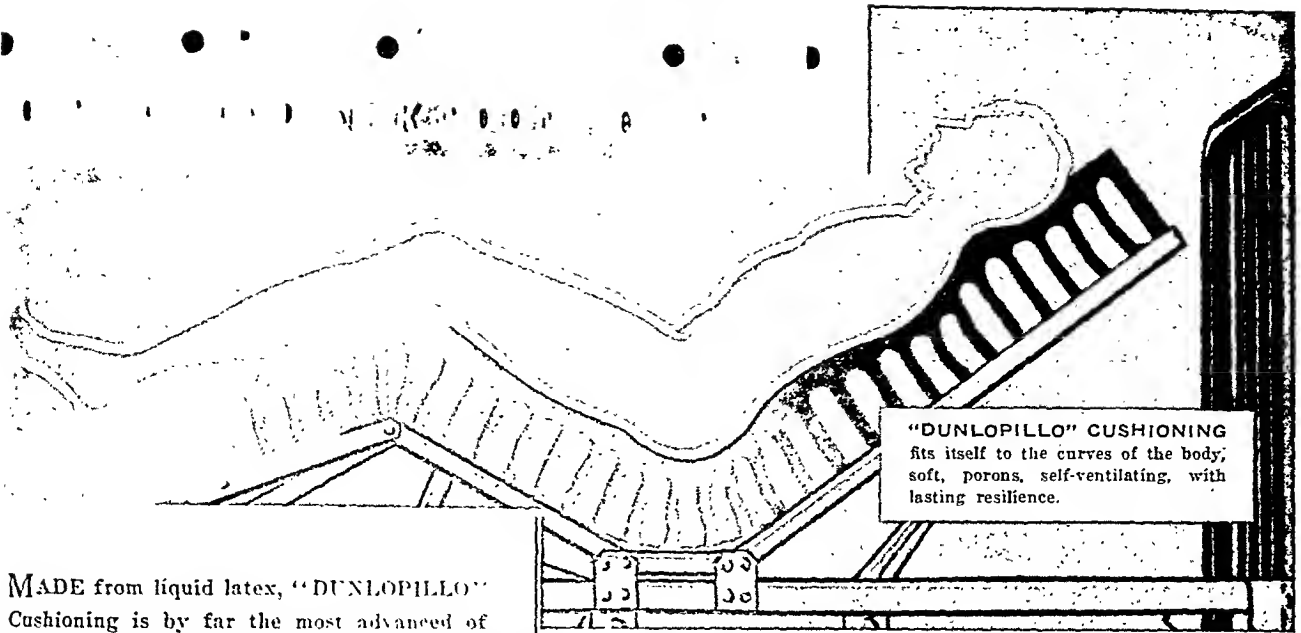
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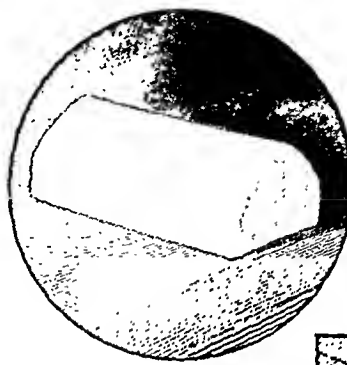


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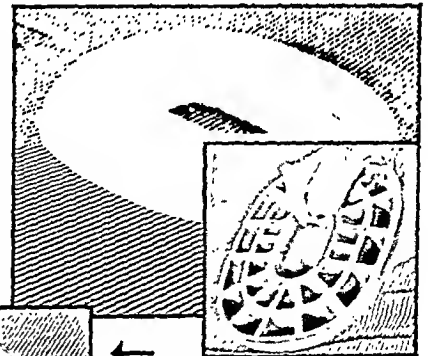
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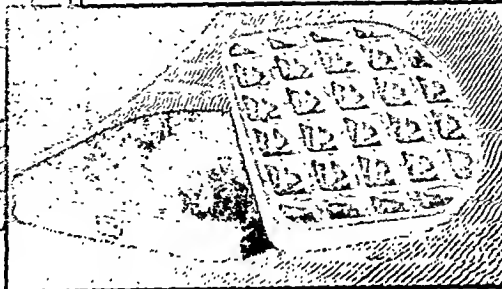


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3. Odorless and dustless—made of latex, not hard rubber.
4. One-piece construction for maximum wear and comfort.
5. Tuftless, no springs, no padding—can't lump, break down or sag.
6. Durable—latex from which it is made has natural life and resilience.
7. Light weight, due to high porosity. Contains millions of interconnected air cells.
8. Naturally aseptic—moth proof and vermin proof.
9. Easily moved for change or storage when not in use—does not deteriorate.
10. Stable, yet luxuriously comfortable.
11. Washable in soap and water, or lysol solution.
12. Economical—lasts for years. Backed by Dunlop's world-wide reputation.

Ask your hospital supply house or write direct to Dunlop for complete information.

DUNLOP TIRE & RUBBER GOODS CO. LIMITED - TORONTO



HE'S DEPENDING ON YOU TO RECOMMEND THE BEST!



THERE can be no compromise with quality when you're prescribing the diet for this little fellow! His foods must be the finest attainable—absolutely dependable, high in nutrient content, and superbly appetizing. That's why increasing numbers of physicians everywhere rely on Heinz Strained Foods for the infants in their care!

Famous For Quality

Heinz Strained Foods are prepared according to a quality tradition that has made the 57 Varieties famous for purity, uniformity, and flavour since 1869. The choicest fruits, vegetables, meats, and cereals in the land are cooked, strained, and packaged *scientifically*. Thus valuable vitamins and

minerals are retained to an unusually high degree!

Freshness Guaranteed

You can be *sure* of the freshness of Heinz Strained Foods. Every tin is stamped with the date of manufacture. And all Heinz Strained Foods remaining on dealers' shelves after a limited time are exchanged for fresh products.

Remember, too, Heinz Strained Foods bear the important Seal of Acceptance of the American Medical Association's Council on Foods! And they cost no more than ordinary brands.

Heinz Strained Foods are prepared at the company's plant in Leamington, Canada. Sample tins will be gladly sent free for your investigation. Address H. J. Heinz Company, Toronto, Ont.



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TWO SEALS
THEY MEAN
PROTECTION FOR
BABY

HEINZ STRAINED FOODS

12 KINDS—1. Beef & Liver Soup. 2. Strained Vegetable Soup. 3. Mixed Greens. 4. Tomatoes. 5. Carrots. 6. Beets. 7. Spinach. 8. Prunes. 9. Apricots and Apple Sauce. 10. Cereal. 11. Peas. 12. Green Beans.

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EVEN without previous experience, YOU can make extremely accurate electrocardiograms with a minimum of manipulation and at small expense with the entirely new light-weight, low-priced G-E Electrocardiograph.

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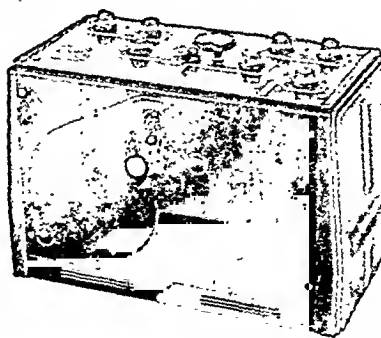
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How closely do you modify?



PHYSICIANS prescribe little unmodified cows' milk for feeding young infants for the good reason that the composition of cows' milk differs widely from that of human milk. As you know, most young infants cannot tolerate whole cows' milk.

It is possible to modify cows' milk in the home kitchen, but the extent of modification is limited. Under kitchen conditions one may prepare a formula in which the percentage of protein and carbohydrate, to some extent, approach those of human milk, but it is still far from being an adaptation to breast milk, particularly from the qualitative side. In addition, such mixtures contain decidedly less of the important food constituent, fat.

Why not go further in your modification? Why not prescribe S. M. A. which is modified under technical control to the point where its physical and chemical constants are essentially similar to breast milk?

S. M. A. resembles breast milk not only in percentages of protein, carbohydrates, fat, and

ash, but also in the chemical constants of the fat and in physical properties. In prescribing S. M. A. you know that even the buffer curve, the hydrogen ion concentration, electrical conductivity, and depression of the freezing point are almost identical with those of breast milk.

And, in addition, S. M. A. has always contained enough cod liver oil to prevent rickets and spasmophilia, and the vitamin A activity of S. M. A. is constant and uniform every month of the year, unlike cows' milk, fresh or evaporated.

Thousands of physicians prescribe S. M. A. routinely because in most cases S. M. A. produces excellent nutritional results simply and quickly.

Prescribe S. M. A. for your next feeding case and compare the nutritional results with those obtained by other methods. S. M. A. is available in almost every prescription pharmacy in the United States.



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Theelin (ketohydroxyestratriene) for intramuscular administration, and Theelol (trihydroxyestratriene) for oral use, are chemically pure estrogenic substances rigidly standardized by physiological and chemical methods. To facilitate proper dosage, the following package forms are available:

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Supplied in 1-cc. Ampoules in boxes of 6, 25 and 100. (Ampoules No. 182 in boxes of 6 and 50.)

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IS IT Gout?

IS IT Arthritis?

Soreness, stiffness, slight enlargement of the phalangeal joints (other joints may be involved), impaired motility, or progressive loss of function . . . particularly manifested about middle-age—such is the symptom-picture many cases present.

It suggests a case of gout, or one of arthritis. . .

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given per os in teaspoonful doses, once or even twice daily, usually brings about prompt amelioration of the condition, and, if administered persistently, often a complete disappearance of all symptoms.

LYXANTHINE ASTIER so acts by virtue of its associated synergists—Iodine, Calcium, Sulphur, Lysidine bitartrate*; the latter a powerful solvent and eliminant of metabolic waste.

*Ethylene-ethenyldiamine.

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BATHING OTITIS

There are four major types of ear conditions resulting from bathing

①

Polluted water may irritate or infect the epithelium lining the external ear canal and outer surface of the drum—a dermatitis of the ear canal.

②

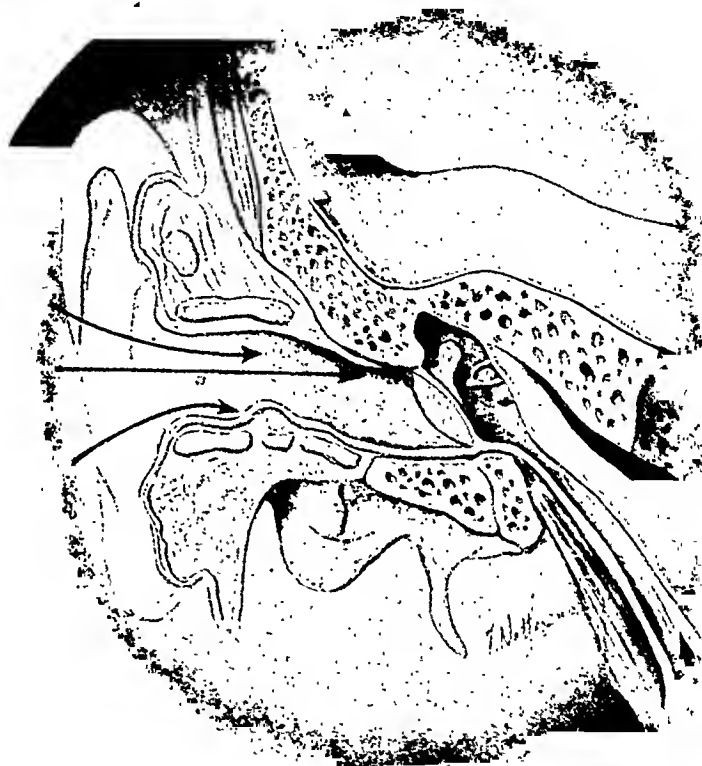
The impact of a forceful wave may produce a traumatic irritation of the drum—a traumatic myringitis.

③

A furuncle or furunculosis of the ear canal may result if organisms from contaminated water work their way through the epithelium.

④

Finally, a true and often vicious otitis media may develop if infectious water enters the nose or mouth and then passes by way of the Eustachian tube to the middle ear.



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(Made in Canada)

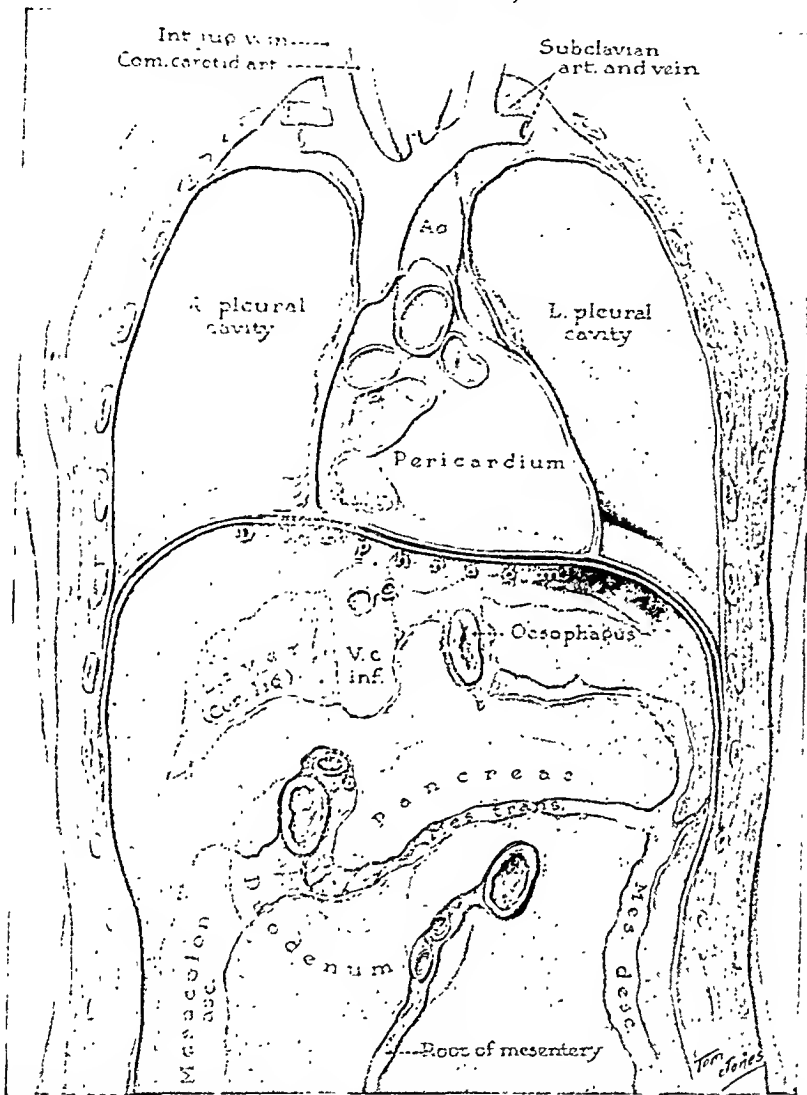
In all four varieties of so-called bathing otitis, great benefits accrue from the early and intensive use of AURALGAN. The external canal should be carefully cleansed and dried and then filled with AURALGAN every hour or two.

Because of the specially processed, highly hygroscopic glycerol contained in AURALGAN, it takes up moisture from the tissues and relieves edema and congestion. At the same time AURALGAN allays pain and discomfort—but it contains no phenol. For symptomatic and therapeutic improvement in Bathing Otitis—prescribe AURALGAN.

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ANATOMICAL STUDIES

(PLATE LXXI)



RELATION OF DIAPHRAGM TO THORAX AND ABDOMEN



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CANNED FOODS IN THE CONTROL OF LATENT AVITAMINOSIS C

● The identification of cevitamic acid (1-ascorbic acid) as vitamin C served as a direct stimulus for the intensive study of the multiple problems involved in determining the human requirement for this factor. As a result of much extensive work, there have been developed three methods for estimating the intake or store of vitamin C in the body.

The "retention or saturation" test is carried out by administering a massive dose of vitamin C and determining the amount excreted in the urine in a given time (1).

As a second method, the daily excretion of vitamin C in the urine is considered indicative of adequacy of the intake (2).

A third method is the determination of the amount of vitamin C in the blood plasma or serum (3). These tests have been combined in balance studies and may serve as valuable checks in the diagnosis of latent scurvy, when used

separately or in conjunction with the less specific capillary resistance test (4).

Evidence is accumulating from the application of these tests which confirms the older view that acute cases of scurvy are rare in this country. However, this evidence does indicate rather wide occurrence of the sub-clinical forms of scurvy (5).

Correction of this condition is largely a matter of modification of the diet to include more liberal quantities of the fruits and vegetables which are known to be good sources of vitamin C. Recent reports indicate that vitamin C in such fruits and vegetables is afforded a good degree of protection during modern canning operations (6).

Since they are available at all seasons on practically every Canadian market, these canned foods afford a valuable and economical means of controlling latent avitaminosis C.

AMERICAN CAN COMPANY

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AMERICAN CAN COMPANY, LTD. - VANCOUVER

(1) 1935. The Lancet 228-I, 71

(2) 1936. Am. J. Med. Sci., 191, 319

(3) 1935. Proc. Soc. Exper. Biol. & Med., 32, 1930

(4) 1933. J. Lab. & Clin. Med. 18, 484

(6) 1936. J. Nutr. 12, 405

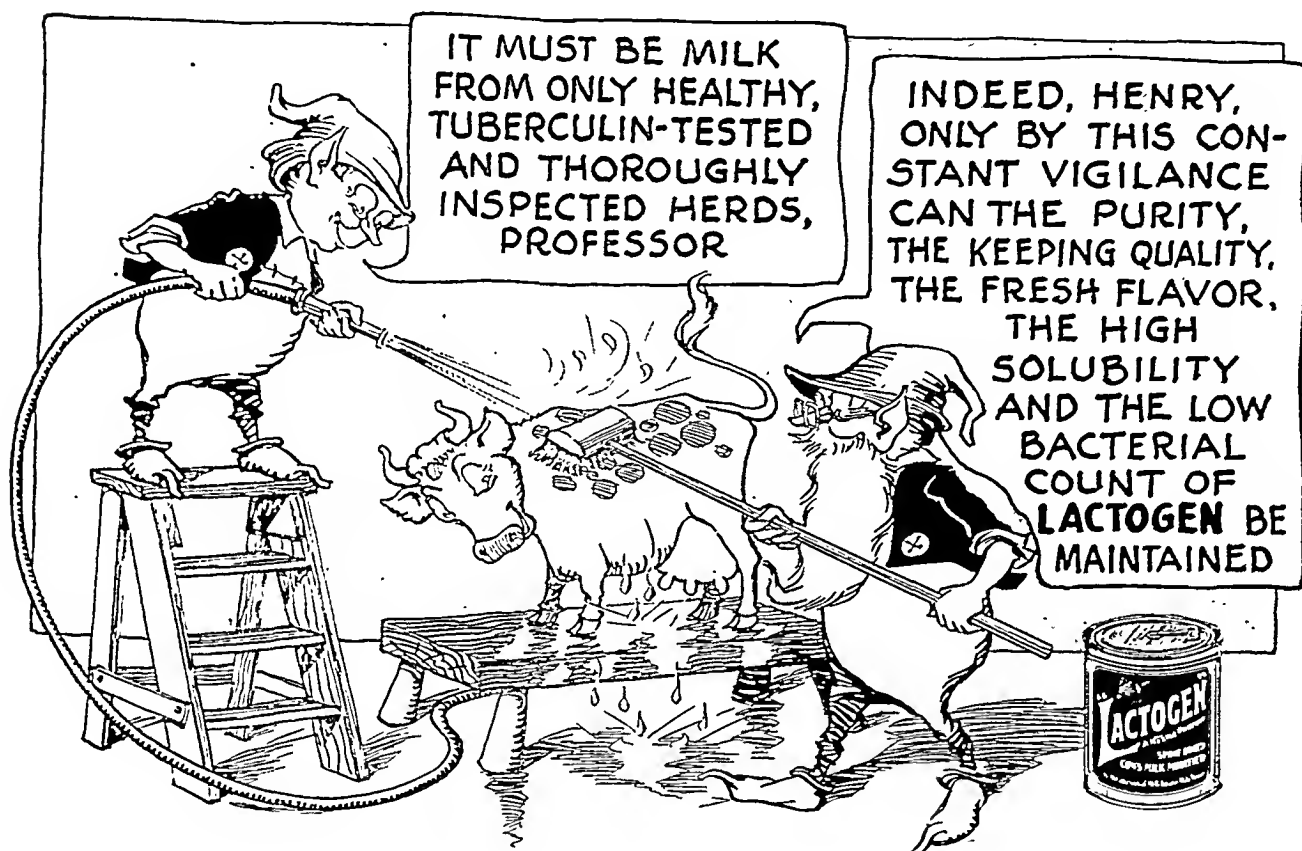
1936. Ibid. 11, 383

1935. Am. J. Pub. Health 25, 1340

(5) 1937. The Avitaminoses
Eddy and Dahldorff
William and Wilkins
Baltimore

LACTOGEN just cannot be made from inferior or old milk

It is impossible to make a high milk-fat, spray dried, modified cow's milk that will "keep"—without extreme care as to the quality of the milk used



Therefore, Lactogen can be made only from High Quality Milk!

FOR Lactogen, with its high milk-fat content, prepared with special avoidance of "drastic heat" by a process never more severe than pasteurization, compels the use of strictly pure, clean, fresh milk of very low bacterial count.

Milk for Lactogen is obtained only from tuberculin-tested herds in regularly-inspected dairies, and is

thoroughly checked for cleanliness and bacterial count before it is accepted. Only by this constant vigilance can the purity, the keeping quality, the fresh flavor, the high solubility and the low bacterial count of Lactogen be maintained.

In other words, both the formula of Lactogen and the milk processing are a definite guarantee to physicians that Lactogen just cannot be made out of ordinary milk. Milk for Lactogen cannot be just "fair"—it must be the highest quality, or Lactogen simply cannot be manufactured commercially.



For Literature and Samples of LACTOGEN, please send professional blank to

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METROPOLITAN BUILDING

CANADA



PERANDREN

"Ciba"

(Testosterone propionate)

Conclusive clinical reports on Perandren are becoming very numerous, and its practical application in a number of conditions and diseases arising from disordered internal secretions in the male, and to a lesser extent in the female, are being well-defined. It has, further, been established that it is desirable to have the product also in higher doses, therefore, besides the 5 mgrm., ampoules containing 10 and 25 mgrms., are now available.

Further, largely increased manufacturing of Perandren has made it possible to reduce the price of the 5 mgrm. ampoules by about 50%, and to establish for the 10 and 25 mgrms. the lowest possible figures.

*Available in
ampoules of 5,
10 and 25 mgrms.*

*Ask today for
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literature.*

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cartons of 3 and
6 ampoules*



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MENSTRUAL TAMPONS

Preferred because they

1. Permit absorption of menstrual discharge at cervix uteri.
2. Eliminate prospect of irritation.
3. Minimize subjection to odorous decomposition products.
4. Reduce danger of infection of perineal origin.
5. Relieve psychological hazard.
6. Provide sanitary protection in its most convenient, comfortable and hygienic form.

The Modern Method FOR MENSTRUAL HYGIENE

CHAPTER 1

TAMPAX

Permits Absorption of
Menstrual
Discharge at Cervix Uteri...

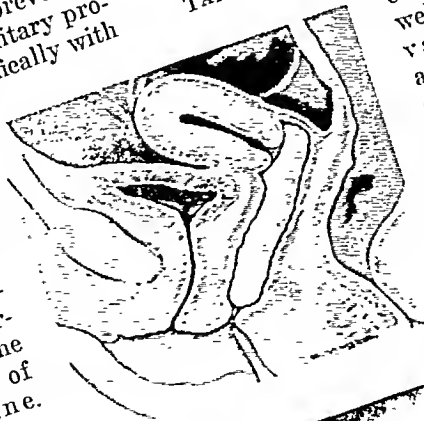
IT IS EASY to understand the primitive failure to differentiate between uterine and vaginal function, and the tendency to consider the menstrual flow a product of the genital tract as a whole.

Even in later years, although menstruation has long been recognized as fundamentally a uterine phenomenon, the lack of adequate means has prevented the employment of sanitary protection designed specifically with that physiologic fact in mind.

TAMPAX menstrual tampons were designed by a physician, with an authoritative understanding of the requirements of true hygiene.

They recognize the menstrual flow as of uterine origin, and permit its absorption at the point of discharge—i.e., at the cervix uteri—before exposure to the outside air has had a chance to provoke the odorous decomposition of blood elements. For normal women, this modern method is convenient, safe and effective. Made of long-fibre surgical cotton so stitched that it cannot disintegrate, each TAMPAX is provided with its own

applicator for easy insertion well up in the vaginal canal, and its own cord for gentle removal. Both applicator and used TAMPAX may be readily disposed of.



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Your Prescription for **ASPIRIN** Assures You

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The clinical effectiveness of Aspirin in the control of pain and fever has been established and proven many times during its 38 years of usage.

Insist on Aspirin for the full therapeutic effect.

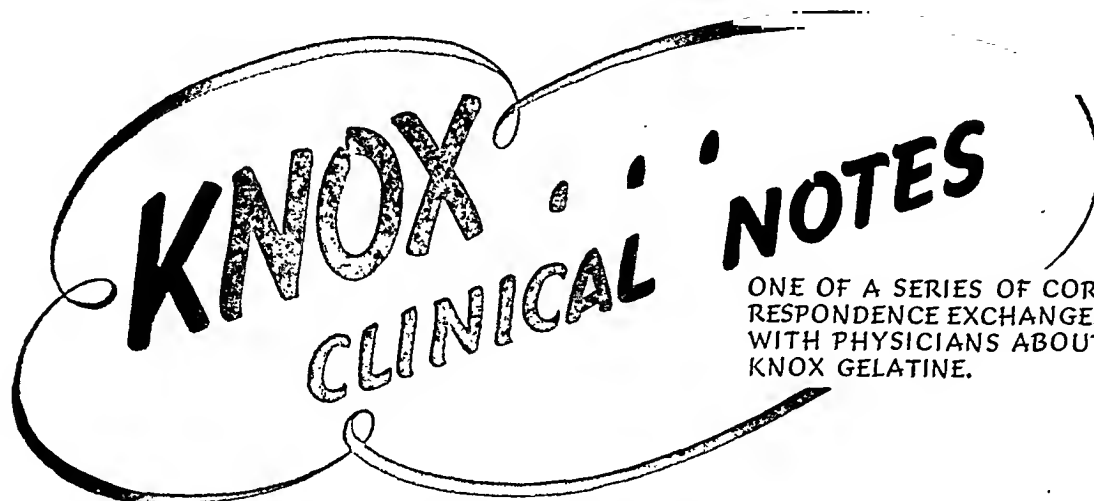
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ONE OF A SERIES OF CORRESPONDENCE EXCHANGES WITH PHYSICIANS ABOUT KNOX GELATINE.

The Glycine Content of KNOX GELATINE

A physician writes, "Pertaining to Glycine—glycocol $\text{NH}_2\text{CH}_2\text{COOH}$ —gelatine contains large amounts of Glycine. I feed a great deal of Knox Gelatine to patients suffering from fatigability—'muscle exhaustion'—with very good results in conjunction with the administration of 15 to 30 grams of Glycine given daily. Glycine is rather expensive to patients—about eight dollars per pound. I wish to know the percentage of Glycine in your best grade Knox Gelatine so I may substitute more liberal feedings of Knox Gelatine and cut the pure Glycine dosage down to a lower and more economical level."

The KNOX GELATINE LABORATORY

Replied as Follows:

Thank you, Doctor! You are right about Knox Gelatine. Increasing amounts of it are being fed in asthenic conditions. Knox Gelatine contains 25% of amino-acetic acid (Glycine). Goodly amounts can be fed in soups, broths, and other recipes to supply amounts of Glycine in this palatable gelatine form which is so economical. Perhaps the simplest way to feed it is as follows:

Sample and useful Dietary Booklets
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"THE KNOX MILK STIR"

Place the contents of 4 envelopes of Knox Gelatine in an ordinary drinking glass. Add 4 ounces of cold milk and allow to soak for five minutes. Add 2 more ounces of milk and stir until homogeneous. Then place glass in small cooking kettle of hot water until gelatine milk mixture liquefies. Add 2 more ounces of cold milk, which will bring the temperature to a satisfactory warm drink of about body heat. A tablespoonful of prune juice or a few drops of any bland flavor like vanilla may be added.

Total: 8 ounce liquid—about 250 calories

Why you should insist on Knox Sparkling Gelatine

Because Knox Gelatine is 85% protein in an easily digestible form—because it contains absolutely no sugar or other substances to cause gas or fermentation, Knox Gelatine should not be confused with factory-flavored, sugar-laden dessert powders. Knox is 100% pure B.P. gelatine. Knox Gelatine has been successfully used in the dietary of convalescents, anorexic, tubercular, diabetic, colitic, and aged patients.



KNOX SPARKLING GELATINE
IS PURE GELATINE—NO SUGAR
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To those seeking only REST and RELAXATION, The Preston Springs offers a place of quiet refinement and unobtrusive friendliness, where the beautiful five-acre gardens surrounding the building may be enjoyed and a good night's rest may be had in comfortable beds.

Located sixty-five miles from Toronto and 195 miles from Windsor.

A private SANITARIUM for DIAGNOSIS, CARE, and TREATMENT of all types of MEDICAL CASES. Its equipment is complete with scientific diagnostic appliances, and employs all forms of therapeutic methods, under the care of qualified physicians, nurses, dietitian, masseur and masseuse. POST-OPERATIVES, RHEUMATICS, MILD PSYCHONEUROSES, CONVALESCENCE of all kinds, INTOXICATIONS (alcohol and narcotic). GASTRO-INTESTINAL CONDITIONS ARE A SPECIALTY.

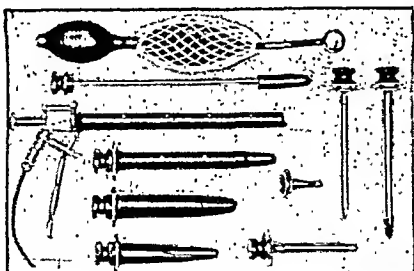
Physicians are invited to visit the institution. Here they will find the highest form of ETHICAL CO-OPERATION. The Preston Springs is licensed as a private hospital by the Hospital Division of the Department of Health, Province of Ontario.

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Every surgeon, gynecologist and general practitioner has felt the need for such a set—that could be used for rectal, vaginal and urethral examinations.

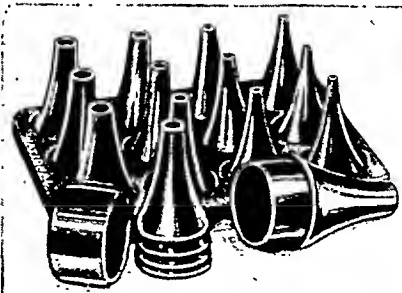
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Includes "Neicomold" Sigmoidoscope, Proctoscope, Child Proctoscope, Anoscope, Tubular Vaginal Speculum, "Virgiscopes", Urethro-scope, Skenescope.

It's a "National"

**"Neicomold"
EAR SPECULA SET**



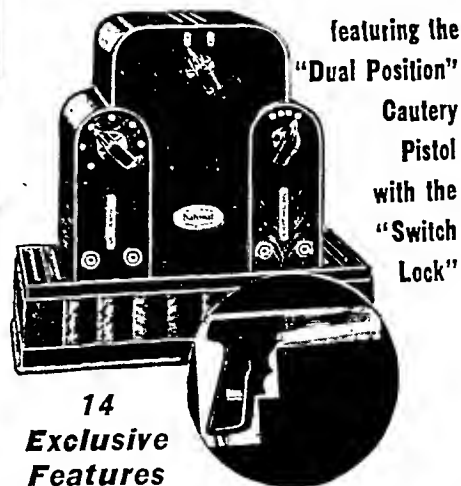
**Complete in Every Detail for
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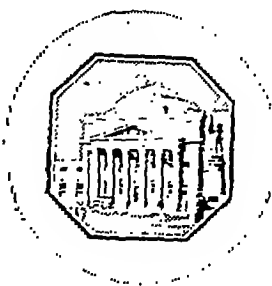
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Specialties

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Limited Registration

Fee \$15.00 for the Course

Includes daily luncheon at the Hospital, a Dinner at the Faculty Club, a Clinical Evening, and other entertainment.

Apply with remittance to—

DR. J. E. DeBELLE, Superintendent
Children's Memorial Hospital, Montreal

Royal College of Physicians and Surgeons of Canada

EXAMINATIONS — OCTOBER 1938

The Primary and Final Examinations leading to the Diploma of Fellow will be held on the following dates:—

Written Examinations in both the Primary and Final subjects on October 3rd, 4th and 5th—in Vancouver, Edmonton, Saskatoon, Winnipeg, Toronto, Montreal, Quebec City, Halifax.

Oral Examinations in the Primary subjects on October 20th in Winnipeg and October 22nd in Toronto.

Oral and Clinical Examinations in the Final subjects on October 24th in Winnipeg and October 26th in Toronto.

Oral and Clinical Examinations in the French Language

In Montreal or Quebec—Dates and place or places to be announced September 1st.

Revision Courses are announced as follows:—

In the subjects of the Primary Examination—

1. Toronto—Departments of Anatomy and Physiology, University of Toronto.
2. Montreal—Departments of Anatomy and Physiology, McGill University.

In the subjects of the Final Examinations—

1. Medicine and Pathology—
Montreal—Dr. W. deM. Sriver, Dr. J. B. Ross, Dr. W. H. Chase.
2. Surgery and Pathology—
Montreal—Dr. R. R. Fitzgerald.

The Annual Meeting of the College will be held in Ottawa on October 29th.

Candidates who are graduates of 1930 or prior thereto of a Medical School or University approved by Council shall not be required to take the Primary Examination, but shall in the Final Examination demonstrate a general and practical knowledge of the clinical application of Anatomy and Physiology.

This special examination shall be conducted by clinicians.

The privilege of this subsection of the Bylaws shall become obsolete on December 1st, 1940.

Address all communications to:

Warren S. Lyman, M.D., F.R.C.P.(C.)
Honorary Secretary,
292 Somerset Street West
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Further details will appear in
subsequent issues.

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MEDICINE—Special Courses during August including Electrocardiography and Heart Disease. Gastro-Enterology in August and October.

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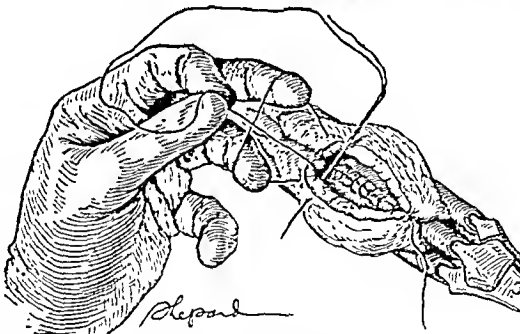
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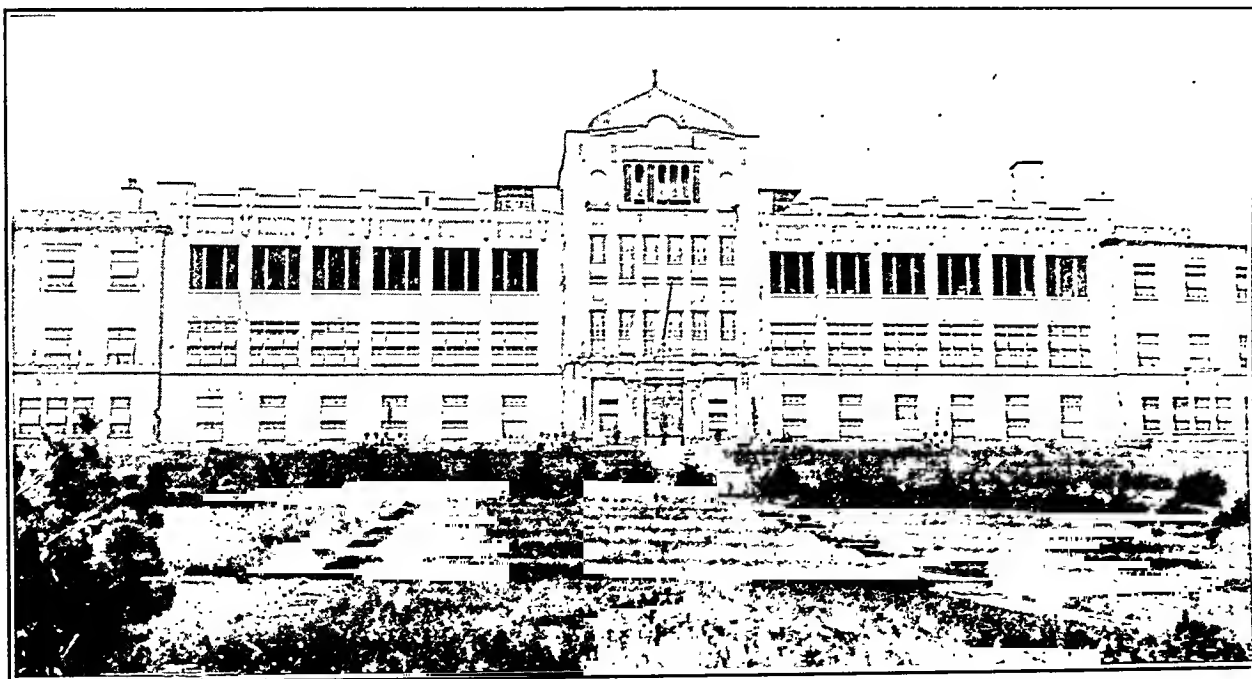
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The Norman Gamble Research Prize, value £50, shall be awarded for the best original work in Otolaryngology completed during the four years previous to the month of October in the year of the award. The competition for this prize shall be open to any British subject, whether lay or medical, who cares to compete, whether or not such persons be holders of or candidates for grants in aid of research.

Grants in aid of research work in Otolaryngology may be made to any British subject, lay or medical, who may be recommended by the Committee of Award to receive such grants, whether or not such person be a holder of or a candidate for the Norman Gamble Prize. Moreover, such grants may be given either to persons who apply for a grant in order to carry out a specific piece of work, or to selected workers chosen by the Committee of Award to carry out certain specified work of its selection.

Any person to whom a grant in aid of research is made from this Fund shall, within such time as may be allowed by the Committee of Award, render a typewritten or printed Report in the English language on the work which has been carried out under the grant, and the Committee of Award shall have the right to publish such Reports.

The Committee shall not make any recommendation either for the award of the Norman Gamble Prize or for any grant in research if the papers of work under consideration are not a sufficiently high standard.

The Committee of Award will consider applications for the Prize and for grants in aid of research work in October 1938.

Applications for the prize and for grants in aid must be received by the Secretary of the Royal Society of Medicine, 1, Wimpole Street, London, W.1., England, not later than September 30th, 1938, and must be in accordance with the regulations stated above.

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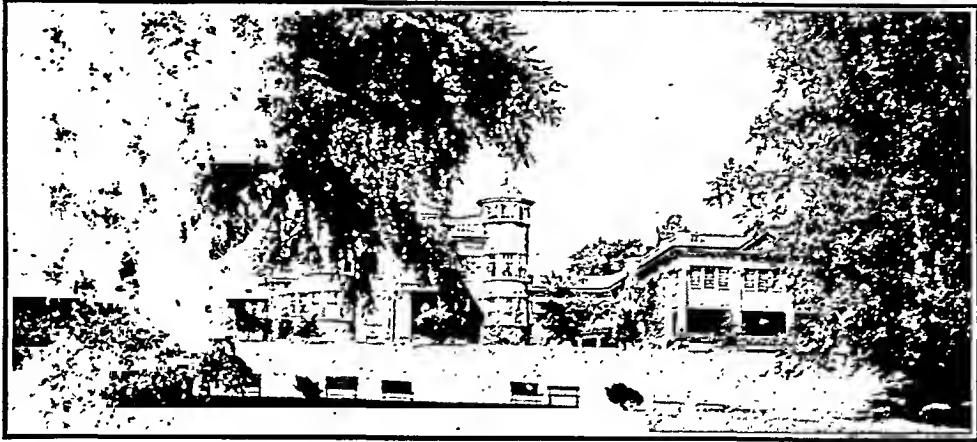
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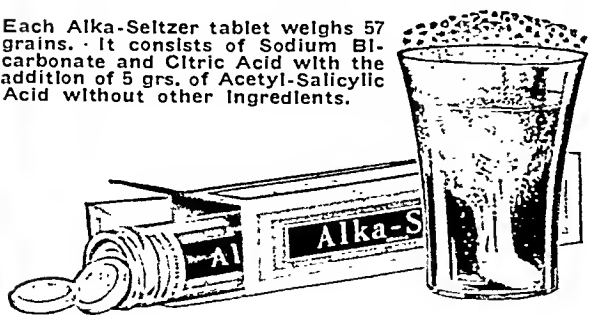
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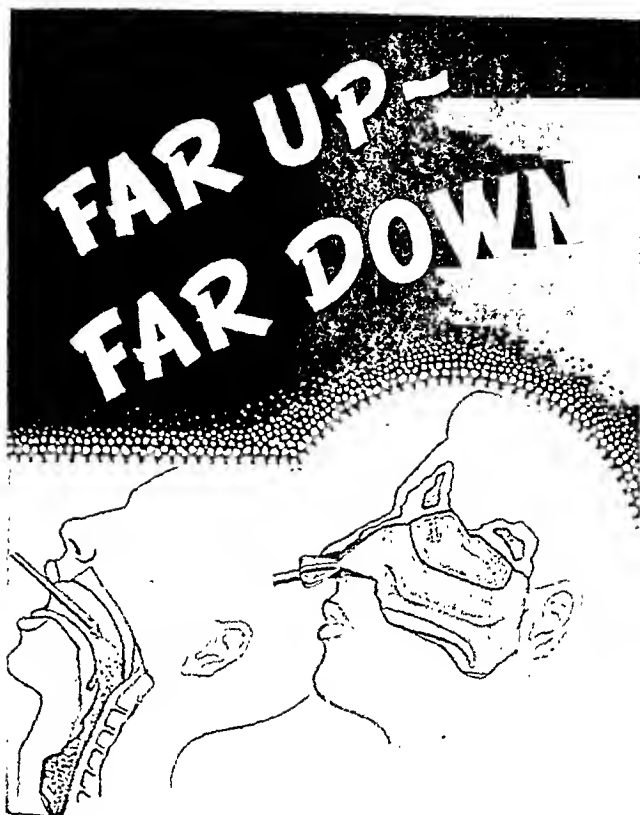
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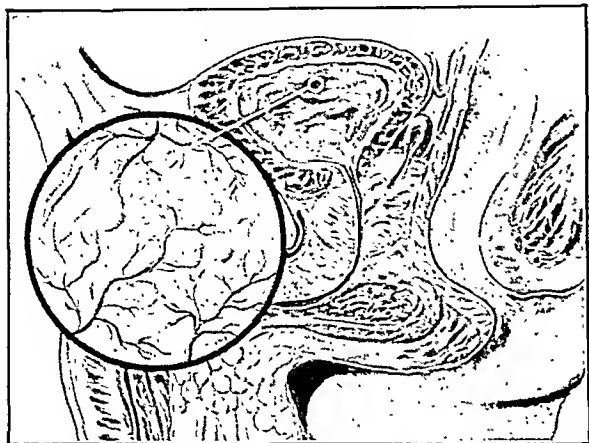
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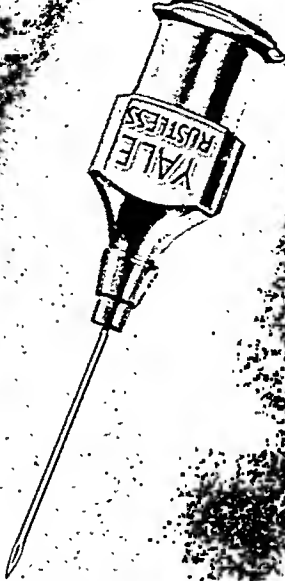
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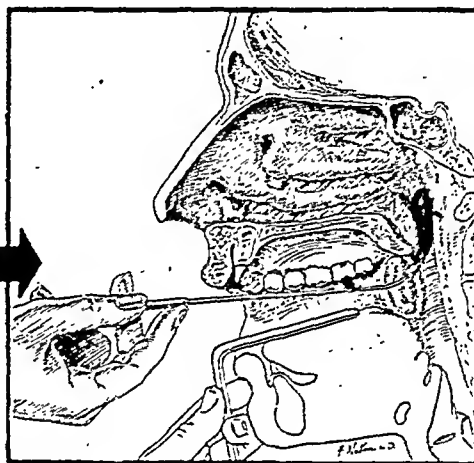
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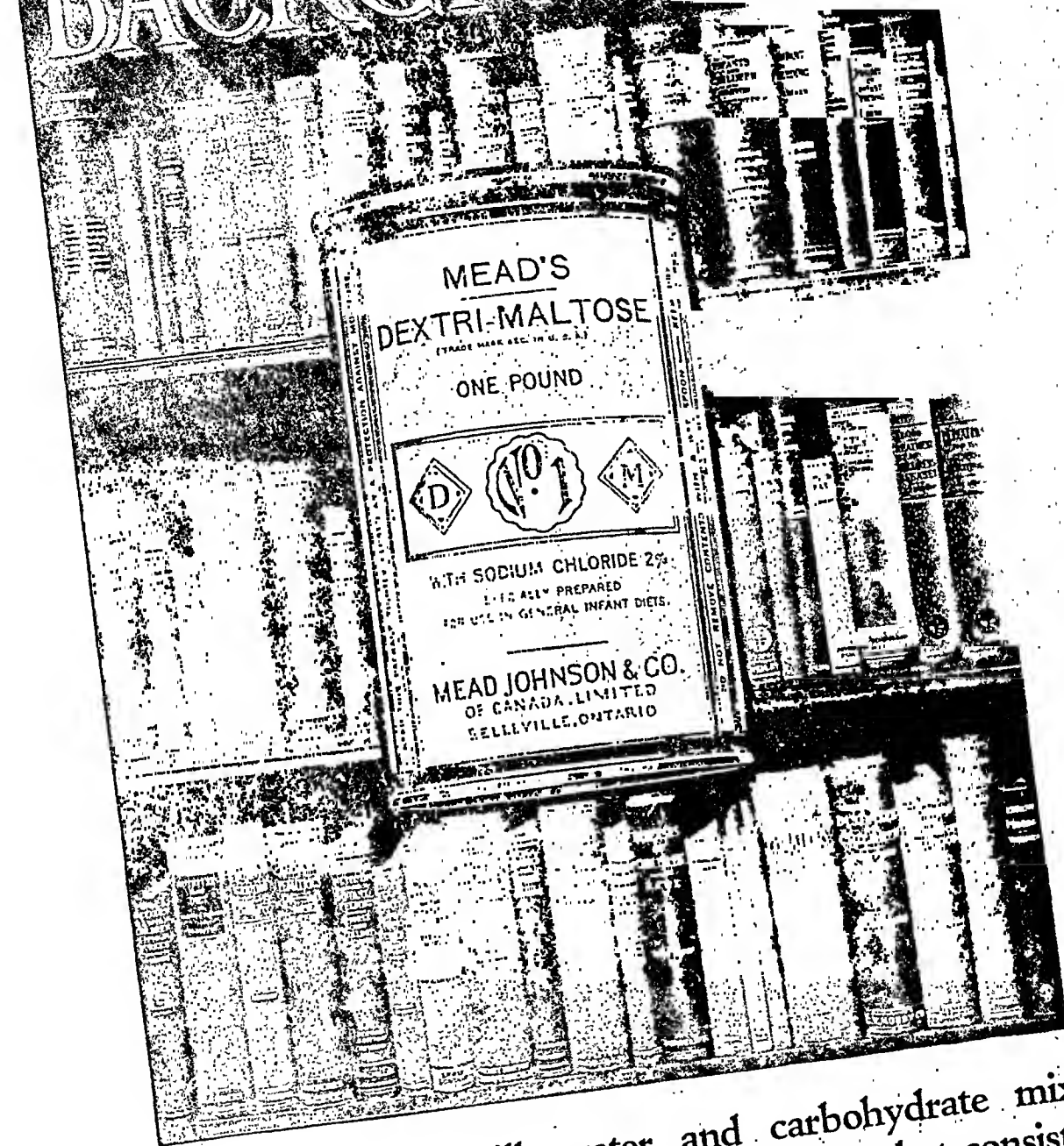
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3640 University Street, Montreal

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AUGUST, 1938

No. 2

Contents

	Page		Page
Acute Anterior Poliomyelitis. II. <i>H. H. Hyland, W. J. Gardiner, F. C. Heal, W. A. Oille and O. M. Solandt</i>	105	Large Solitary Cysts of the Kidney. <i>S. A. Wallace</i>	140
The Human Response to Single Doses of Sulphanilamide. <i>C. C. Lucas</i>	111	Recurrent Intra-Ocular Hæmorrhage in Young Adults (Eales' Disease). <i>S. H. McKee</i>	142
A Pathological Interpretation of Some Surgical Procedures Adopted for the Relief of Glaucoma. <i>F. T. Tooke</i>	114	A Trial Study of 1,800 Cases of Syphilis Infected Twenty Years ago. <i>F. S. Burke and M. Parks</i>	145
The Need for Prolonged Artificial Respiration in Drowning, Asphyxiation and Electric Shock. <i>G. Bates, R. E. Gaby and W. MacLachlan</i>	120	The Significance of Epigastric Hernia. <i>J. C. Luke</i>	149
The Percutaneous Tuberculin Reaction. <i>H. P. Wright, A. F. Chaisson and R. Allison</i>	123	Points of Mutual Interest to the General Practitioner and the Radiologist. <i>W. A. Jones</i>	152
Cardiac Lesions in Adrenal Insufficiency. <i>G. E. Hall and R. A. Cleghorn</i>	126	The Psychiatrist's Point of View. <i>J. D. M. Griffin</i>	157
The Relation of Pregnancy to Biliary Disease and the Control of the Vomiting of Pregnancy. <i>J. M. McGown and J. O. Baker</i>	133	On the Value of Correcting the Red Cell Sedimentation Rate for the Effect of Cell Volume. <i>D. W. Crombie and A. Hambleton</i>	162
Changes in the Olfactory Mucosa and the Olfactory Nerves Following Intranasal Treatment with One Per Cent Zinc Sulphate. <i>C. G. Smith</i>	138	Miliary Tuberculosis in a Newborn Infant. <i>G. M. White and D. F. W. Porter</i>	165
		The Department's Responsibility for Food Protection. <i>R. E. Wodehouse</i>	167
		CASE REPORTS	
		Acute Rheumatic Fever with Unusual Complications. <i>H. S. Good and B. Kance</i>	170

CONTINUED ON PAGE IV

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CONTENTS CONTINUED FROM PAGE II

	Page	
Simultaneous Bilateral Spontaneous Pneumothorax Complicating Bronchial Asthma. <i>G. S. Jeffrey and D. C. Marlatt</i>	171	MEDICAL SOCIETIES
Chronic Acne Vulgaris (Indurata) in Middle-Aged Women. <i>A. H. Pirie</i>	171	American Association of Anatomists
THERAPEUTICS AND PHARMACOLOGY		Canadian Medical Association—Alberta Division
The Treatment of Constipation. <i>H. G. Bird</i>	172	Canadian Physiological
Paroxysmal Tachycardia. <i>W. F. Connell</i>	173	Nova Scotia
EDITORIAL		Regina General Hospital
The Halifax Convention	174	Saskatoon City Hospital
Vitamins and Cancer	175	Tri-County
The Value of Artificial Respiration	176	Western Nova Scotia
EDITORIAL COMMENTS		POST-GRADUATE COURSES
Sunlight and the Skin	176	University of Toronto
The Purpose of Organization of the Canadian Society for the Control of Cancer	177	Information for Doctors in Berlin
SPECIAL ARTICLES		MEDICO-LEGAL
Insulin Therapy in the Future of Psychiatry. <i>M. Sakel</i>	178	Diversion of Gift from American to English Hospitals
Diet and Nutrition		TOPICS OF CURRENT INTEREST
Vitamins in Infancy and Childhood. <i>F. F. Tisdall</i>	179	Benzedrine Sulphate—A Warning
MEN AND BOOKS		Freshmen Grow in Stature
Early Vaccinations in British North America. <i>R. C. Stewart</i>	181	Mosquito Bites
ASSOCIATION NOTES		ABSTRACTS FROM CURRENT LITERATURE
The Halifax Annual Meeting	183	Medicine
Valedictory Address by Dr. T. H. Leggett, Retiring President	184	Surgery
HOSPITAL SERVICE DEPARTMENT NOTES		Obstetrics and Gynaecology
A New List of Canadian Hospitals Approved for Internship	187	Therapeutics
		Radiology and Physiotherapy
		Pathology and Experimental Medicine
		Hygiene and Public Health
		OBITUARIES
		W. C. Acheson 198
		A. A. Backus 198
		B. C. Blackhall 198
		F. Boulanger 199
		W. A. Cathcart 199
		T. J. Costello 199
		A. R. Cunningham 199
		J. L. Easton 199
		A. Falardeau 199
		J. B. Fraser
		J. A. Gallagher
		T. S. Kirby
		A. J. MacKinnon
		M. D. Moyse
		W. C. Pepin
		M. C. Roberts
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		NEWS ITEMS
		Canada 200
		Book Reviews

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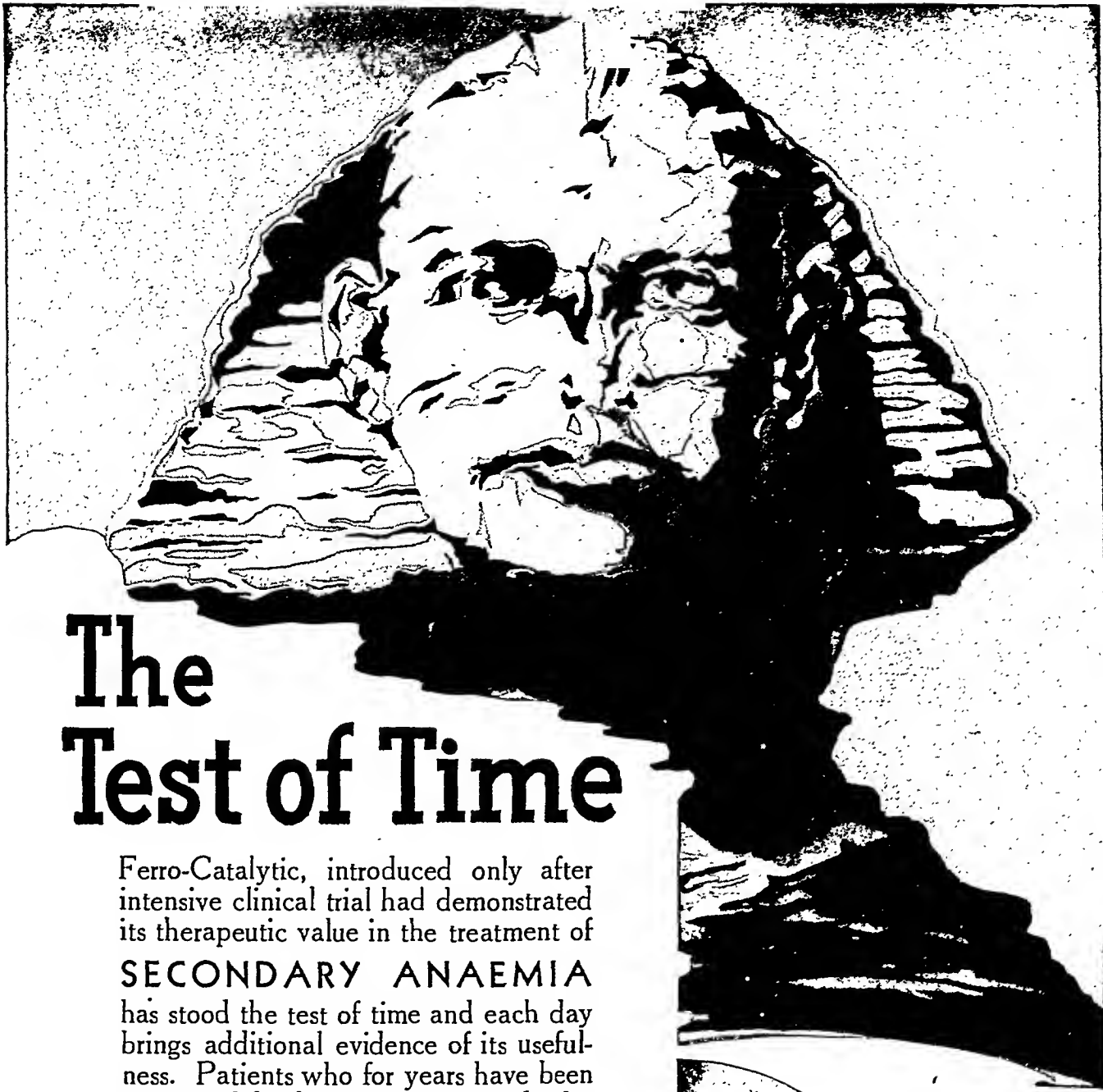
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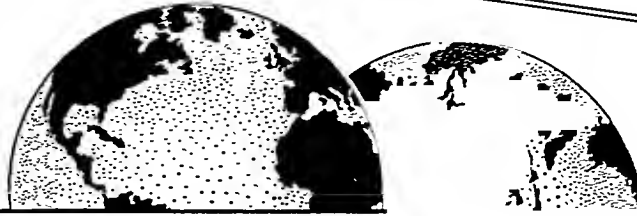
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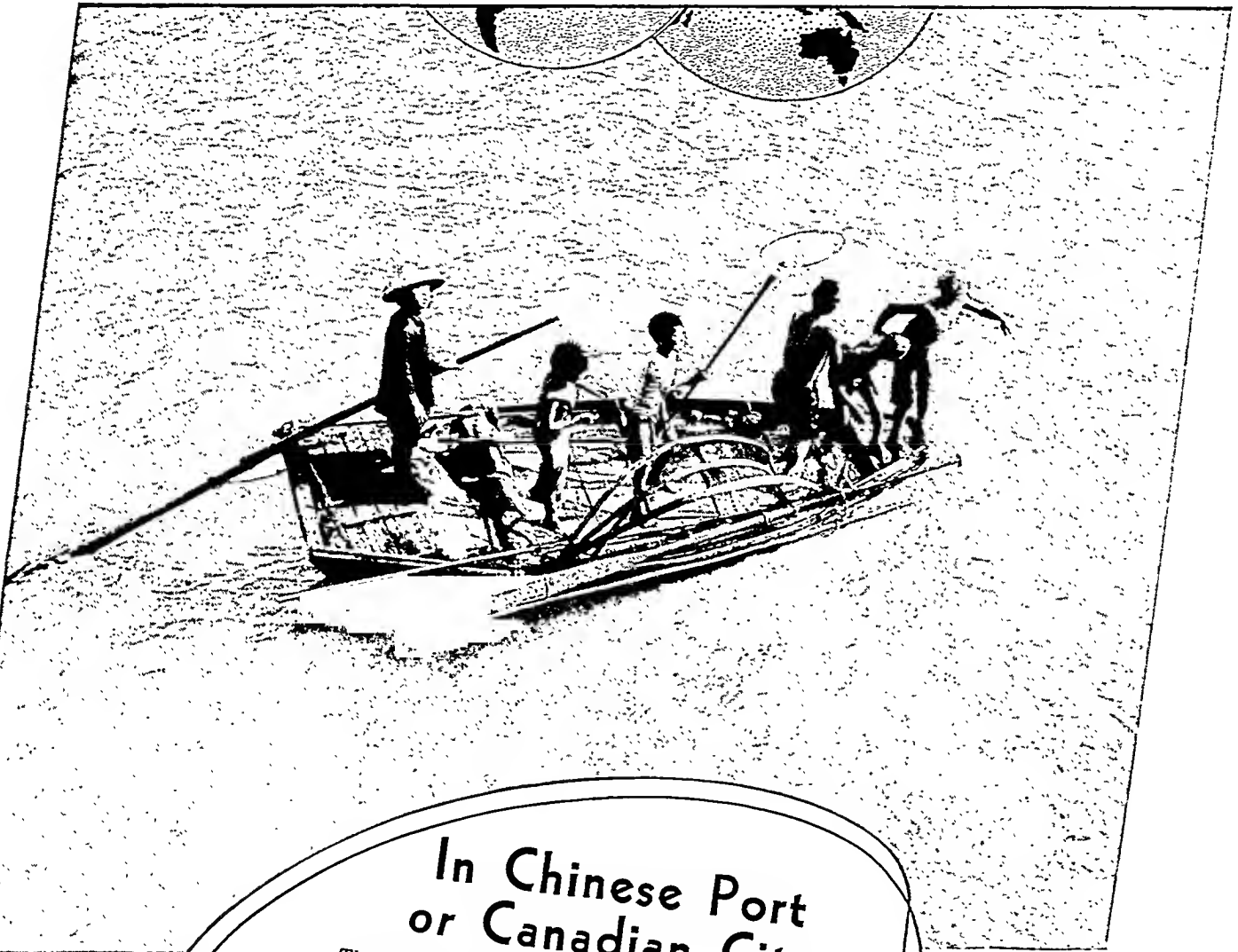
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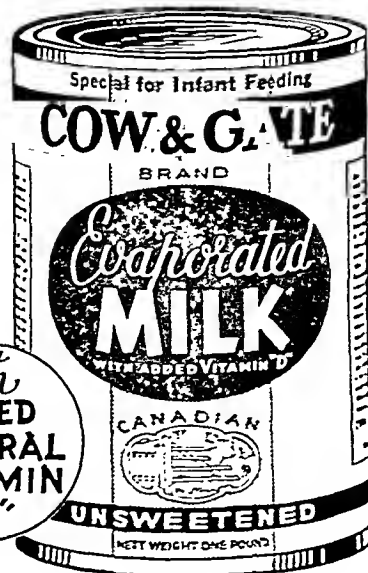
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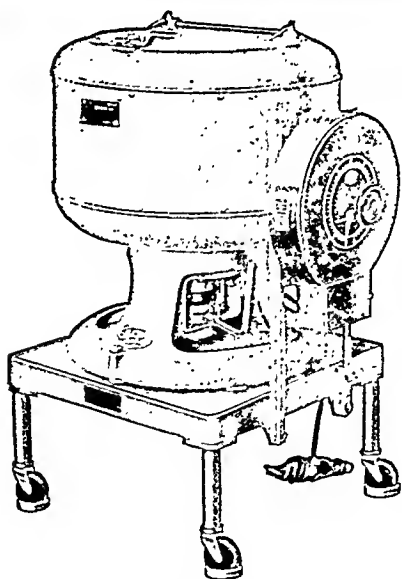
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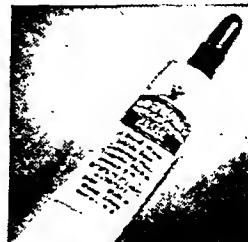
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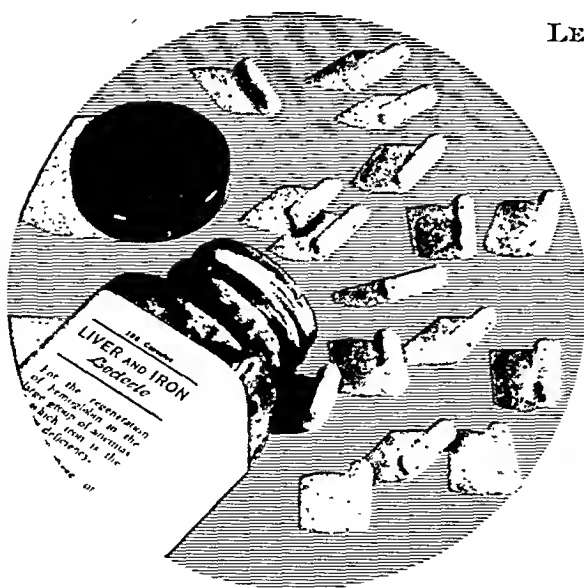
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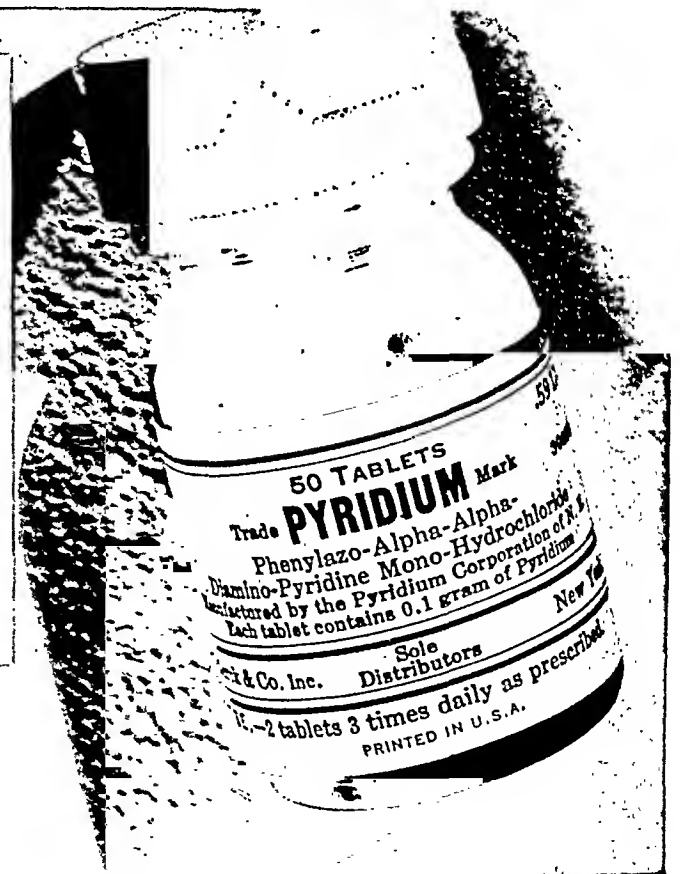
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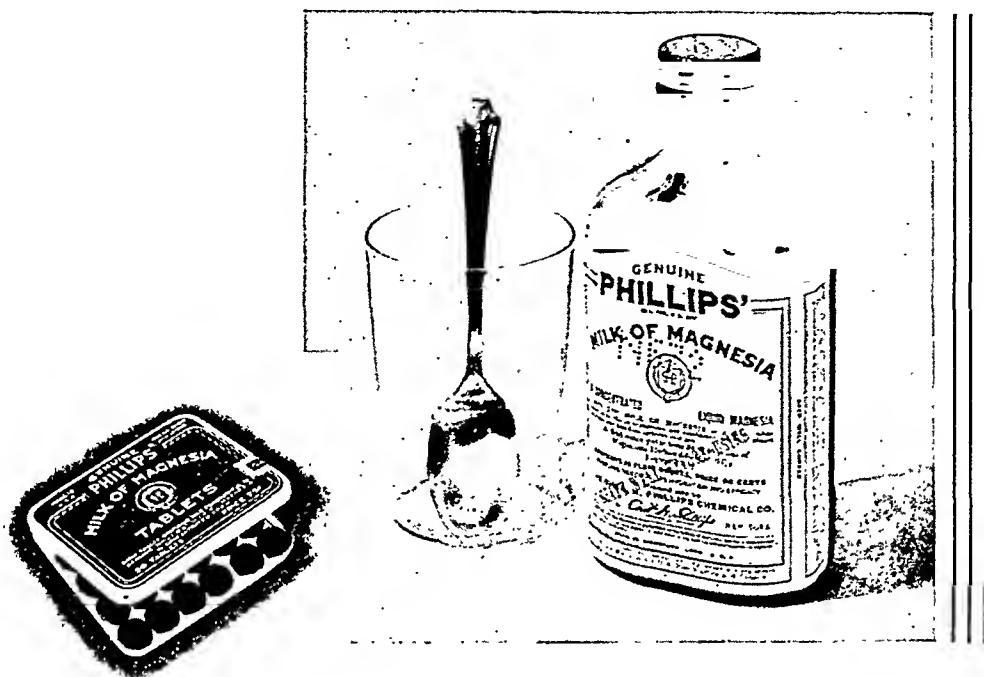
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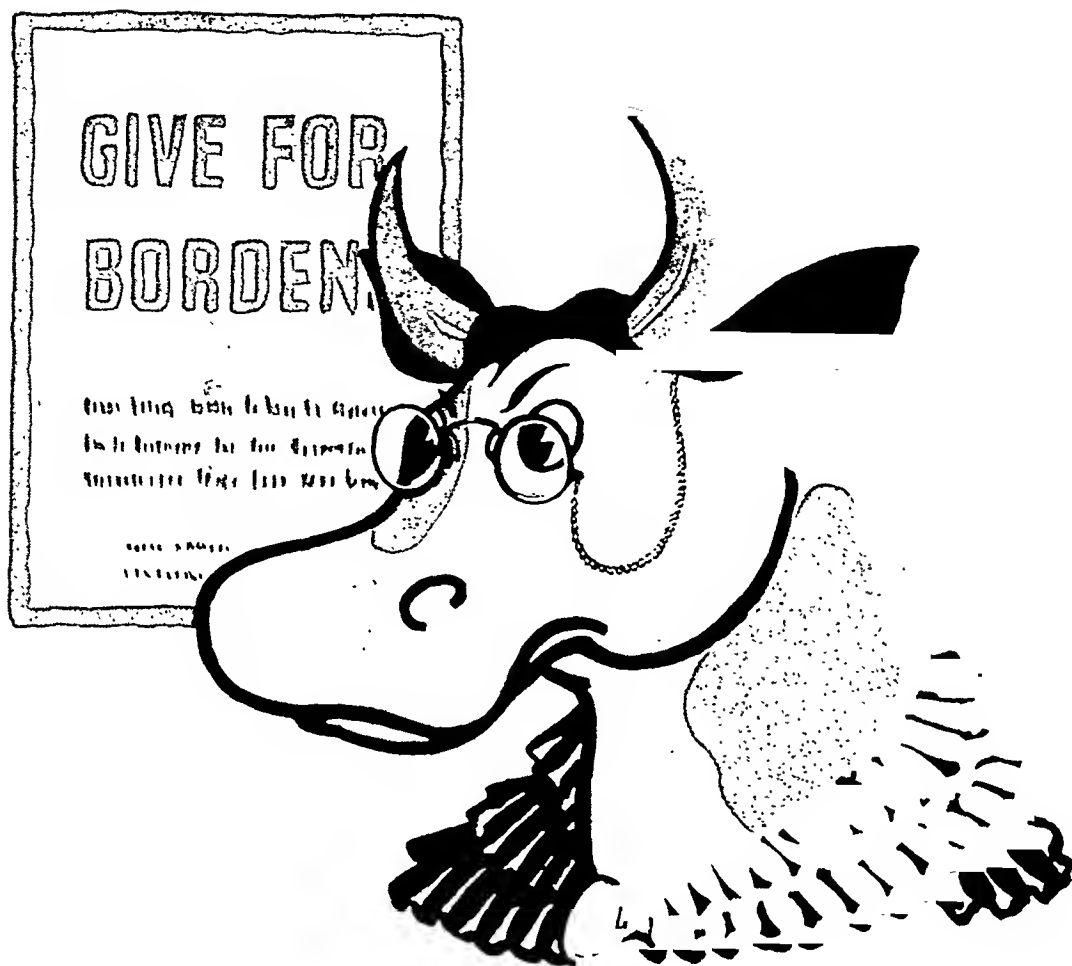
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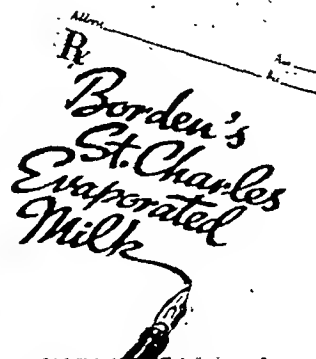


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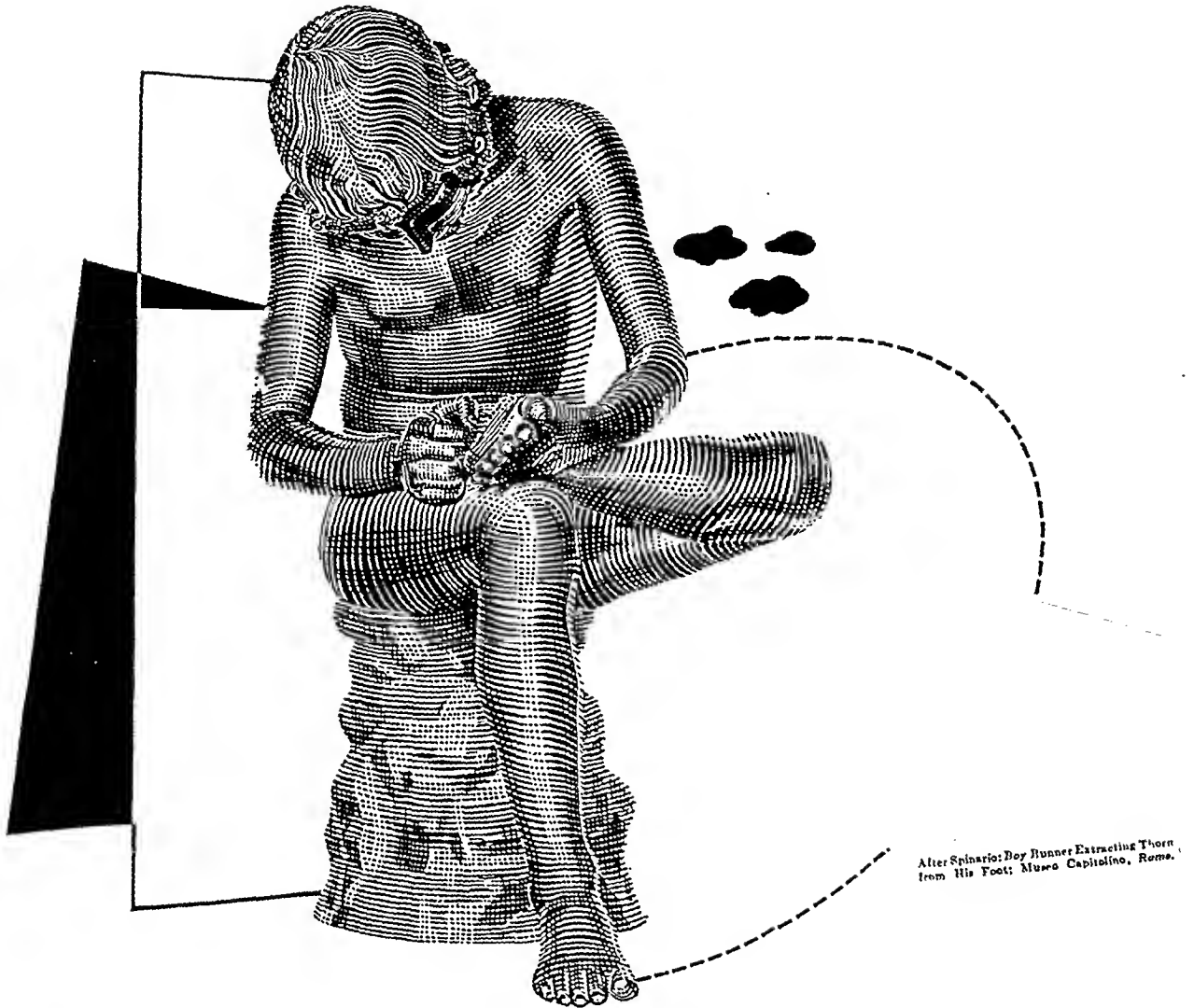
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The Canadian Medical Association Journal

Vol. 39

TORONTO, AUGUST, 1938

No. 2

ACUTE ANTERIOR POLIOMYELITIS*

(A REVIEW OF SIXTY-SIX ADULT CASES WHICH OCCURRED IN THE 1937 ONTARIO EPIDEMIC)

BY H. H. HYLAND, W. J. GARDINER, F. C. HEAL, W. A. OILLE AND O. M. SOLANDT

Toronto

II.†

THE RESULTS OBTAINED IN TREATMENT OF PARALYZED CASES TO DATE, AND A CONSIDERATION OF CERTAIN METHODS EMPLOYED

Respiratory paralysis.—In this series 16 patients were given respirator treatment. Ten of these had bulbar involvement as well as paralysis of respiratory muscles. Seven died soon after being placed in a respirator. The remaining 9, including 4 bulbospinal cases, are alive at the time of writing, approximately six months from the onset of illness. One, who was only in a respirator for three days, has shown steady recovery of respiratory power and is now approaching normal. Three others have recovered sufficiently that they no longer require the aid of a respirator for even part of the day. Five are still receiving respirator treatment; two of these will probably be out of the respirators within a few months. The remaining three will require respirator treatment for many months, although they are already out of the respirators from one to four hours daily.

In observing the patients with paralysis of respiratory muscles it was soon found that only gross changes in respiratory capacity could be detected by ordinary clinical methods of examination. With a view to obtaining more accurate records of the progress of paralysis of the respiratory muscles estimations of vital capacity¹⁷ were made. All vital capacity determinations were made with the Benedict-Roth basal metabolism apparatus, which has proved very

satisfactory for the purpose. Determinations can be made without upsetting even the most severely paralyzed patients, because the respirator need be turned off for only a few breaths, and during that period the patient breathes a high concentration of oxygen from the spirometer. No difficulty was encountered in getting the cooperation of the patients, except in a few cases during the first few days of the illness. During recovery the patients soon came to anticipate the test, and were so keen on breaking their previous record that there was no difficulty in getting them to do their best.

It would have been valuable to have made serial determinations of vital capacity on all cases of poliomyelitis, whether they showed signs of respiratory difficulty or not. Unfortunately time did not permit this. Determinations were only made when some weakness of the respiratory muscles was suspected from clinical observation. If the first test showed a diminution in vital capacity, or if there was progress of the paralysis, the estimations were repeated. In those cases in which the respiratory paralysis demanded respirator treatment an attempt was made to estimate the vital capacity daily for a time, and then weekly during the period of recovery. Long series of vital capacity determinations have been made on 8 patients. These give a fairly accurate picture of the progress of recovery of the respiratory muscles. Chest measurements and fluoroscopic examinations were done on these patients at intervals, but

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† For Part I see this *Journal*, 1938, 39: 1.

were not found to be as satisfactory or as accurate an index of improvement as were vital capacity estimations. The vital capacity curves for five of the patients are reproduced here. (Figs. 1 to 5). A brief summary of the history

of each case is given under the corresponding graph.

Fig. 1 (case H.B.) is presented to show how rapidly the recovery of respiratory power may take place. Recovery of power in the paralyzed

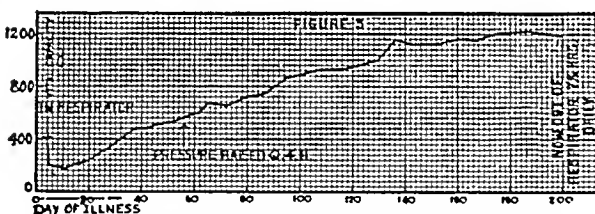
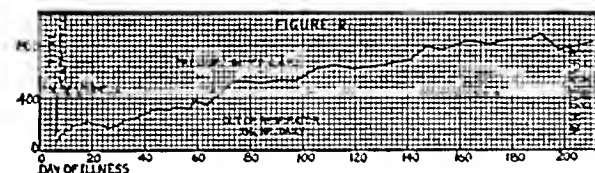
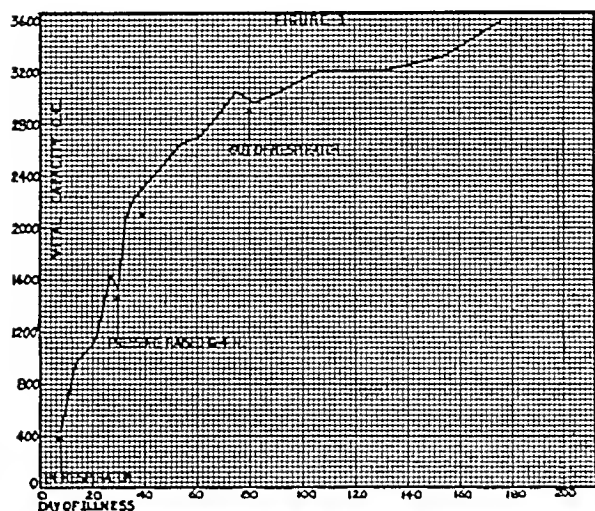
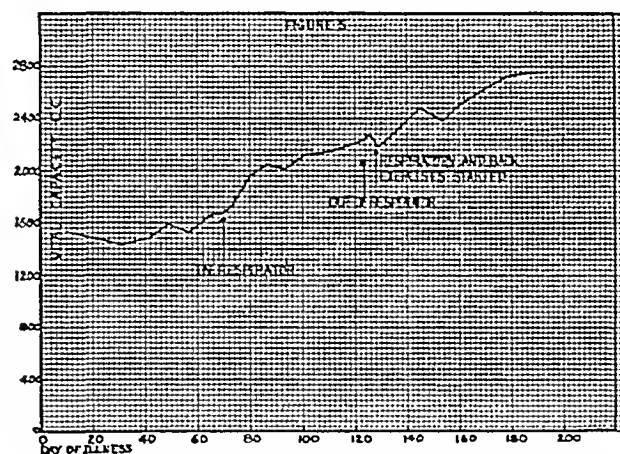
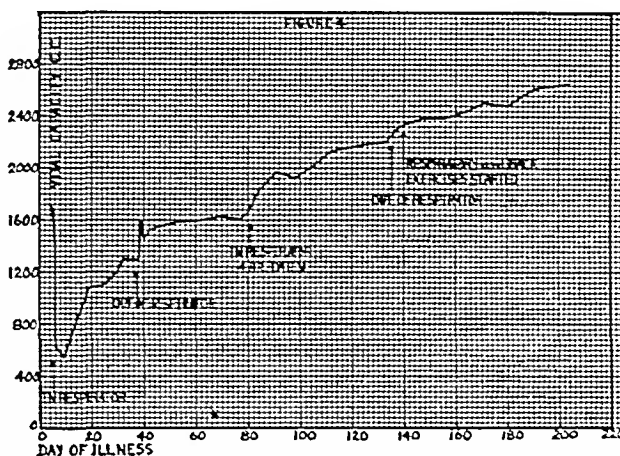


Fig. 1.—H.B., male, aged 19; normal vital capacity 4,900 c.c. Onset of illness October 6, 1937. Admitted on 7th day of illness. Placed in a respirator immediately. Recovery was very rapid. He could be out of the respirator for seven hours at a time by the 21st day. Pressure in the respirator was increased for one minute every four hours, starting on the 31st day. He could be out of the respirator twelve hours daily by the 50th day. Respirator treatment was discontinued on the 80th day. Exercises to increase mobility of the spine were started on the 110th day.

Fig. 2.—G.G., male, aged 24; normal vital capacity 4,150 c.c. Onset of illness August 30, 1937. Admitted on the 6th day of illness. Placed in respirator immediately. Recovery has been very slow. He was able to be out of the respirator, without the administration of oxygen, for ten to fifteen minutes by the 57th day. Pressure in the respirator was increased for one minute every four hours, starting on the 68th day. The patient was allowed to remain out of the respirator for half an hour three times a day by the 80th day. He is now (after 200 days) out of the respirator for one and a half hours three times a day, and has been receiving daily passive exercises to the spine for the past seventy days.

Fig. 3.—G.K., male, aged 16; normal vital capacity 3,800 c.c. Onset of illness September 10, 1937. Admitted to hospital on September 12th; placed in respirator September 13th. Recovery has been well maintained in spite of much intercurrent illness.



Pressure in the respirator was increased for one minute every four hours, starting on the 57th day of illness. He was able to remain out of the respirator for half an hour by the 35th day and for one hour three times a day by the 83rd day. Passive movements of the spine were begun about the 150th day. He is now (after 200 days) out of the respirator two and a half hours three times a day.

Fig. 4.—J.C., male, aged 29; normal vital capacity 4,300 c.c. Onset of illness September 6, 1937. Admitted to hospital September 10th; placed in respirator immediately. Recovery was quite rapid, and respirator treatment was discontinued on the 38th day of illness. Subsequent recovery of vital capacity was not satisfactory, so the respirator treatment was resumed for four hours daily, from the 51st to the 125th day. Respiratory exercises and active exercises to increase mobility of the spine were begun about the 139th day.

Fig. 5.—W.S., male, aged 26; normal vital capacity 4,550 c.c. Onset of illness September 17, 1937; admitted to hospital, September 20th. He complained of some respiratory distress by the 7th day of illness. Since this did not progress he was not placed in a respirator. When his vital capacity failed to increase satisfactorily he was given respirator treatment for four hours daily, from the 71st to the 123rd day of illness. Respiratory exercises and active exercises, to increase mobility of the spine, were begun about the 126th day.

limbs in this case was very satisfactory but was not nearly so rapid as was the increase in vital capacity.

Fig. 2 (case G.G.) shows a very much slower rate of recovery. Two other cases showed a comparable rate of recovery. In all three there was very severe paralysis of skeletal muscles with slow recovery.

An intermediate rate of recovery is shown in Fig. 3 (case G.K.). This curve is remarkable for its steady rise. Recovery pursued a fairly constant course in spite of severe digestive disturbances and alterations in regimen designed to increase the rate of progress.

Patient J.C. (Fig. 4) made a very satisfactory recovery, and was removed from the respirator after thirty-one days of treatment. Following an increase in the first day or two out of the respirator his vital capacity remained almost unchanged for six weeks. In an attempt to accelerate the rate of recovery this patient was returned to the respirator on the eightieth day of his illness for four hours daily. Following institution of this treatment his vital capacity improved considerably, and, later, when respirator treatment was discontinued the improvement was maintained.

Patient W.S. (Fig. 5) showed some respiratory weakness early in his illness, but was not put in a respirator because his vital capacity was never greatly reduced. His subsequent recovery of respiratory power was extremely slow. On the seventy-first day after the onset of his illness he was put in a respirator for a four-hour period. This treatment was continued daily and his vital capacity showed steady improvement which was continued when respirator treatment was discontinued later.

The experience with these cases suggests that the patient J.C. was removed from the respirator too soon (vital capacity 1,300 c.c.) on the first occasion, and that patient W.S. might have benefited from earlier respirator treatment even though his vital capacity never fell below 1,300 c.c. With these observations in mind other cases received respirator treatment until their vital capacities reached at least 2,000 c.c. This rule will probably have to be modified in the more severe cases where the ultimate vital capacity may be less than 2,000 c.c.

In treating paralyzed respiratory muscles it is logical to follow as far as possible the plan of treatment carried out in other cases of paralyzed

muscles. The patient with respiratory paralysis is put in a respirator primarily to save his life. However, once the acute stage of the disease is past, the respirator not only keeps the patient alive but also supplies the first two essentials of treatment—rest and passive movement. Later, as the patient recovers, active movement is encouraged by allowing him to breathe for himself and by having him do breathing exercises.

It is difficult to be sure that the respirator really does rest the muscles of respiration and the nerve cells that supply them. The intercostals and diaphragm are not analogous to other skeletal muscles, because the nervous impulses to the muscles of respiration are not ordinarily under voluntary control. One observation suggests that the respirator does rest the muscles of respiration. If a patient with a vital capacity of about 400 c.c. is put in a respirator and the pressure adjusted so that the tidal air is about 400 c.c., the patient, if asked to breathe with the machine, can increase the tidal air considerably, occasionally up to 700 c.c. or more.

In a patient with severe paralysis of the intercostal muscles the ribs fall into a position of complete expiration. This is borne out by the fact that it is almost impossible to ventilate such a patient by prone pressure artificial respiration, because the thorax cannot be further compressed. Unless there is very early return of muscle power the costo-vertebral articulations will stiffen just as other joints do when immobilized, and rib movement will be permanently limited. Limitation of movement at other joints is readily overcome by manipulation. Unfortunately passive movement of the ribs cannot be performed by the physiotherapist. However, there is evidence that periodic increases in the negative pressure in the respirator, by increasing the tidal air far above the resting level, can move the ribs. That this rib movement helps to free the ribs and allow the weakened muscles to move them further is shown by the permanent increase in vital capacity which followed such treatment in some of the patients. This increase is best seen in case G.G. (Fig. 2). At the point marked "pressure raised Q 4H" the negative pressure in the respirator was raised for one minute every four hours from 12 cm. of water, which was his ordinary maintenance pressure, to about 25 to 30 cm. of water. This gave a ventilation of about 1,200 c.c. per breath.

Further evidence of the therapeutic effect of respirator treatment is shown by the marked increase in vital capacity which occurred when the patient W.S. (Fig. 5) was first put in the respirator and when the patient J.C. (Fig. 4) was returned to the respirator after having been out for six weeks. In both cases respirator treatment was only carried out for four hours a day and the negative pressure was increased to 25 to 30 cm. of water one minute in every hour. It could be argued that the increase in vital capacity was due to the four hours' rest. However, it is our opinion that the real cause of the improvement was the passive movement of the ribs, just as in the case of G.G. (Fig. 2), where there was no question of increased rest.

This brief discussion emphasizes the fact that the respirator is not only a means of keeping the patient alive by supplying adequate artificial respiration but is also the most important factor in treating the paralyzed respiratory muscles by rest and passive movement. Breathing exercises and controlled active exercises for the back are important adjuncts to respirator treatment when sufficient recovery has occurred to permit their use.

Non-respiratory paralysis.—More than six months have elapsed since the majority of these patients came under observation. Forty-seven patients suffered paralysis; of these 9 died. The results of treatment in the remaining 38 are summarized in Table VIII.

TABLE VIII.
RESULTS OF TREATMENT IN 38 SURVIVING
PARALYZED CASES

	No. of Cases	Time
Complete recovery	3	1 month
“ “	5	3 months
“ “	2	6 months
Good functional result	2	3 months
“ “	3	6 months
<i>Prognosis in remaining 23 cases:</i>		
Good functional result	8	3 months
“ “	2	6 months
Fair outlook for good functional result (including 3 respirator cases)	5	1-3 years
Poor outlook for good recovery of function (all respiratory cases)	5	
Seriously paralyzed but no longer under observation at the To- ronto General Hospital	3	

It will be seen that fifteen patients, 39 per cent of the survivors, have had a complete recovery or have obtained good functional use of the paralyzed muscles in the six months

they have been under treatment. Ten other cases, 26 per cent, are progressing so favourably that a good functional result is anticipated within the next six months. Of the 13 cases where the ultimate result is doubtful at the present time 8 are respiratory cases and the majority of these would have died soon after admission had there not been facilities for treatment such as were available in this epidemic.

To date our patients have been kept at rest in bed until the return of power in the affected muscles has been sufficiently advanced to permit strong voluntary movement against gravity. Later it may be considered advisable to allow certain patients to become ambulatory with the use of braces or other devices, to compensate for paralysis, but so far improvement has been so satisfactory that this has not been seriously thought of in any case.

A detailed analysis of the response of individual muscles to treatment will not be attempted at this time. However, sufficient observation has been made on certain methods of treatment to permit a few comments in regard to their application. Early splinting of limbs in severely paralyzed cases is beneficial, providing passive movements of the joints are carried out daily and careful observation made to ensure that the support given certain paralyzed muscles by the splint is not jeopardizing the recovery of other muscles which are stretched by the position that is being maintained. Whereas splinting may often be of aid in counteracting the development of contractures the immobility it involves sometimes leads to them. To prevent contractures assuming serious proportions it is necessary to have flexible splints which permit easy alteration of shape. The splinted limbs should receive frequent treatments with massage, heat and passive movement from the first, to prevent the development of contractures, or gentle forced movements to overcome them if they have already developed.

Although splinting may be of great value in the treatment of severely paralyzed muscles it can be continued too long. When return of power has occurred to a degree which permits full range of voluntary movement against gravity, even though the movement is weak, recovery is usually more rapid after discarding the splint. This does not mean that the weak muscles should be subjected to continuous

stretching, but at this stage other methods of support, such as pillows, sandbags and slings, are preferable because they allow a certain amount of movement of muscle fibres, thereby improving muscle tone and the circulation to the limb. Following removal of splints we have seen rapid return of power and improvement in atrophy in several instances.

That certain severely paralyzed muscles can make excellent recovery without the use of splints or limitation of active movement was shown in one of our patients. In this case the anterior, posterior and lateral neck muscles were severely paralyzed, and marked atrophy had occurred. The patient was of a restless temperament and interested in all that was happening around him. No limitation was imposed on the movements of his neck, but the fact that he was recumbent, with his head on a pillow constantly, eliminated the possibility of severe stretching of the affected muscles by gravity. The return of power in these neck muscles over the six-month period was as satisfactory as that seen in muscles elsewhere where splinting had been employed. Other examples of good recovery of power were observed in patients with paralysis of muscles supplied by the 5th nerve. Rapid improvement has occurred in all instances with no limitation of active movement having been imposed.

Where the pull exerted by gravity may be detrimental, as is the case in paralysis of many limb muscles, uncontrolled active exercises may result in definite harm and thereby retard recovery. This was demonstrated in one of our cases with paresis of the left shoulder girdle. The patient was not splinted and active movements were allowed. A control case with a comparable and similarly situated paralysis was splinted. Both patients received the same amount of physiotherapy. The improvement in the splinted case was much more rapid than in the unsplinted case. When the latter received similar support to the paralyzed muscles and uncontrolled active movements were stopped improvement commenced and progressed satisfactorily. Another patient who was admitted to hospital about ten weeks after paralysis developed had been walking on the paralyzed leg with no recovery of power during that time. After complete rest in bed in hospital with support to the paralyzed muscles rapid improvement was noted. Later, controlled active

exercises of the paralyzed muscles were instituted with further improvement.

The progression of wasting in muscles under treatment should not cause undue anxiety, because marked wasting can occur in affected limbs out of all proportion to the degree of paralysis. This has been noted in the hands particularly and also in other groups of muscles. Wasting often continues for a considerable time after good return of power is evident. The disproportion between wasting and paralysis is sometimes so striking that it seems probable that the wasting is not due to destruction of the anterior horn cells alone; possibly involvement of the lateral horn cells causes nutritional disturbance which contributes to its development.

In an endeavour to estimate the value of early controlled active exercises comparison was made between the results in certain selected cases and in controls; other physiotherapeutic measures, including passive movement and massage, were employed in both groups. Our results indicate that this method of treatment is of great value in hastening recovery of the affected muscles. In cases where it was not used recovery was, on the average, much slower.

In limbs paralyzed for some time early recovery of function in certain muscles may be missed because the patient has lost the capacity for the particular movement. This may be due to the long inactivity and also to less efficient functioning of the involved reflex arcs due to destruction of certain of their cellular elements. Another factor which interferes with the spontaneous recovery of certain individual muscles is the early tendency on the part of the patient to learn trick movements. In their anxiety to make the limbs function patients employ muscles which are relatively unaffected to carry out movements that they ordinarily do not perform, thus compensating in a poor and inadequate fashion. One of the main purposes of muscle re-education is to prevent this tendency to trick movements, because it yields to the establishment of habits in the pattern of nervous impulses which, when well fixed, are difficult to eradicate. The object in treatment is to concentrate the attention of the patient on the individual movements of the muscles which it is desirable to re-establish. Gradually it may be possible for the surviving cells of the affected lower reflex

ares to conduct the necessary impulses from the brain to the muscles.

Many examples of the value of muscle re-education have been noted in this group of cases. It requires great perseverance on the part of the patients and the physiotherapists to obtain the best results, especially if trick movements have become established. It is important, therefore, that these exercises should be commenced early in convalescence and that they should be continued until it is definitely established that no further recovery will occur. When this period is reached the ability of other muscles to assist in carrying out the movements of those that are paralyzed may be encouraged, and it is often surprising how effective the ultimate result may be. A good example of this is sometimes seen in the way that the flexor and adductor of the thumb can effectively compensate for a powerless opponens pollicis muscle.

As mentioned above, prolonged immobility and consequent fixation of the spine tends to interfere with the recovery in respiratory cases by limiting the capacity of the thorax to expand on inspiration. It also impairs the recovery of other muscles attached to the spine, particularly the flexors, and care should be taken to prevent its occurrence in all cases. Often the weakness in these muscles is more apparent than real. A patient may be unable to flex the spine because of the fixation which has resulted from several months of lying immobile on a Bradford frame; following the increased mobility of the spine brought about by back exercises, the functional capacity of these muscles improves markedly. Even where definite weakness of back muscles is present recovery occurs more rapidly after the introduction of controlled active movements of the spine. When recovery is advanced the use of a Balkan frame on the patient's bed, with a sliding hand grip, is a useful means of facilitating exercise of the back muscles without strain.

Since the improvement of paralyzed muscles in poliomyelitis is known to continue over a period of years, a detailed consideration of the recovery of individual muscles in both respiratory and non-respiratory paralysis has not been attempted here. It is hoped to make this the subject of a future report.

SUMMARY AND CONCLUSIONS

1. A survey of the symptoms, signs, treatment, and results of treatment at the end of

approximately six months in 66 adult cases of poliomyelitis admitted to the Toronto General Hospital during the 1937 Ontario epidemic is presented.

2. Forty-seven patients had evidence of paralysis and 19 were not paralyzed. Eighteen of the paralyzed patients showed involvement of the respiratory muscles. There were 9 fatal cases, of which 8 died of respiratory failure.

3. The sense of smell was tested in 30 cases of poliomyelitis during the acute phase of the illness, using an olfactometer (Elsberg). The results showed that no impairment in the sense of smell was associated with the disease in these cases.

4. The important symptoms and physical signs at the onset of the disease are described, and the cerebrospinal fluid findings are summarized. It is emphasized that the cell count may alter rapidly and that too much reliance should not be placed on negative findings in the fluid in the early stages of the disease.

5. The distribution of paralysis in the 47 paralyzed cases is analyzed, and it was found that the muscles of the left upper limb were involved most frequently.

6. Six of the 9 fatal cases came to autopsy, all of which had received respirator treatment. The gross pathological findings are briefly discussed. While all cases showed pulmonary involvement with collapse or bronchopneumonia, no gross or microscopic evidence of emphysema was discovered.

7. The immediate treatment of the patients, including those with respiratory paralysis and bulbar involvement, is considered in some detail, with particular emphasis on nursing care and the early treatment of paralysis.

8. A series of serum-treated cases and controls is shown. It was found that the incidence of paralysis and deaths was not essentially different in the cases receiving serum in the preparalytic stage and in those not receiving serum.

9. A detailed account of the methods of physiotherapy employed and a discussion of the efficacy of various methods of treatment in the paralyzed cases are given. The necessity for frequent periodic examinations, using muscle charts, in the convalescent paralytic cases is emphasized. The use of spring balances to record improvement accurately is suggested.

10. The results of treatment of respiratory paralysis with respirators is presented. Of the

16 patients receiving this treatment, including 10 with bulbar involvement as well as paralysis of the respiratory muscles, 9 have survived. Four of these have recovered sufficiently to be able to carry on without respirator treatment.

11. Vital capacity estimations, in addition to chest measurements and fluoroscopic examination, were utilized to follow the progress of these patients. Five patients who received prolonged respirator treatment are cited and graphs are shown of their progress to date.

12. The methods used to overcome the fixation of the costovertebral articulations, which retards recovery in respirator-treated cases, are discussed. The results indicate that these measures hasten the recovery of respiratory function.

13. The results of treatment up to the present time are summarized. Of the paralyzed patients who survived 40 per cent have completely recovered or have obtained good functional use of their limbs. In 26 per cent a good functional

result is anticipated within the next six months. In only 34 per cent of the cases is the ultimate result in doubt.

14. From a study of these cases it is concluded that early and continued controlled active exercises are a very important part of the treatment. The optimum results are obtained if patients receive close observation, such as can be provided best in hospital, with frequent treatment by skilled physiotherapists. By these means the tendency to formation of contractures can be dealt with satisfactorily, and recovery of the affected muscles facilitated, thus rendering less likely the development of serious deformities.

The authors desire to express their sincere thanks to Prof. Duncan Graham for permission to publish these cases and for his constant assistance and advice. We wish to acknowledge the help given in this work by Dr. W. P. Warner and Dr. B. C. Blackhall, and to express our appreciation to the physiotherapists whose unflinching interest and cooperation were such an important factor in the treatment of these cases.

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THE HUMAN RESPONSE TO SINGLE DOSES OF SULPHANILAMIDE*

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THE value of sulphanilamide as a specific drug for the treatment of certain types of infection in both man and animals has become so well known during recent months that there is no necessity to dwell upon its merits or describe its use in this communication. There are, however, at least four questions which still are being asked constantly with regard to this, as with any new therapeutic agent of this type: (1) which organisms are brought under control? (2) what concentrations of the drug are necessary in the body fluids to effect this control? (3) what dosage is necessary to reach and maintain an effective concentration of the drug in the body, and (4) what dangers are associated with the use of the drug at the required dosage? Only by close cooperation between clinicians, bacteriologists and biochemists can we hope to obtain complete answers to these pertinent questions.

One such collaborative study has been in pro-

gress in Toronto for some months. Dr. D. R. Mitchell, of the Department of Urology, and Dr. Philip Greey, of the Department of Bacteriology of the University of Toronto, have been engaged in an investigation of the use of sulphanilamide in infections of the urinary tract, and the writer has been responsible for the biochemical aspects of that research. We hope, in the near future, to be able to give adequate answers to all four of the questions propounded above, but in the meantime, this paper supplies a partial answer to question 3.

Data concerning the effects (on human beings) of any given dose of sulphanilamide on blood and urine concentrations were not available when this problem was commenced. In order to obtain such information the writer took three single doses of 15, 30 and 45 grains (approximately 1, 2 and 3 grams) of a commercial sample of prontosil. These tablets were examined and found to be of the strength and purity claimed for them. Intervals of about two weeks were allowed to elapse between the test doses. The drug was taken, not as a thera-

* The data contained in this paper were presented to the Toronto Academy of Medicine, Pathology Section, at the meeting of March 22, 1938.

Finally, we wish to emphasize that the relationships between dose and tissue fluid concentrations found in this investigation on a healthy subject are not necessarily what would result from the administration of sulphanilamide to sick patients.

SUMMARY

1. The effect of single doses of 15, 30 and 45 grains of sulphanilamide upon the concentrations of this drug in blood and urine of a healthy man have been determined.

2. The concentration of sulphanilamide in the blood is not directly proportional to the dose.

3. Blood concentrations of sulphanilamide above 5 mg. per 100 c.c. are not easily attained (while liver and kidney function are normal), since conjugation and excretion occur rapidly.

4. The proportion of sulphanilamide which undergoes conjugation is not constant, even in one individual.

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A PATHOLOGICAL INTERPRETATION OF SOME SURGICAL PROCEDURES ADOPTED FOR THE RELIEF OF GLAUCOMA*

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IT would be a presumption on my part to insinuate in a title which has been allotted to me that I was about to exhaust this vast realm of ophthalmic surgery in one short address. It would be a further impertinence to suggest that from an experience in clinical surgery or from tabulated statistics I could supply you with conclusions or deductions more worthy than your own. But I may, perhaps, be tolerated if in a more or less sketchy manner I attempt to approach our subject as a pathologist, and, with an interesting series of sections, invite suggestion as to how best in glaucoma certain pathological barriers may be lowered and some problems explained.

In this preamble it is not my purpose to refer at length to the factors entering into the production of glaucoma, except to mention one or two of the more commonly accepted ideas as to the solution of the riddle. But whether this reference applies to the findings of Priestly Smith, with the disproportion of the lens and the cornea in hypermetropic eyes, to biochemical changes occurring in the aqueous of a colloid character, as advanced by Martin Fischer in his work on oedema, to the inception of either a high or low grade of iritis or iridocyclitis from an associated autogenous infection, involvement of the fifth nerve and the sympathetic in their

relationships as vaso-dilators in the neighbourhood of the iris, fibrosis of the pectinate ligament, as advanced by Thompson Henderson, degenerative changes in the iris and ciliary body, the road leads us invariably in one direction, to the filtration angle and to the channels of excretion. And whether these theories are associated with clinical manifestations known as congestive or inflammatory, on the one hand, or the more subtle, non-congestive, non-inflammatory, the so-called glaucoma simplex, on the other, surgical endeavour is invariably directed through one procedure or another in an attempt to interpret lesions as they exist at these points, to substitute alternative processes for pernicious physiological functions as they affect the excretion of the aqueous.

It is superfluous to state regarding the treatment of glaucoma that one must first treat the cause, if such can be determined, and, naturally, this remark applies to the class of cases known as secondary, ocular symptoms following upon some other clinical manifestations appearing earlier in the eye. Take cardiovascular or cardiorenal conditions as examples. If kept under control by a sympathetic and intelligent internist this may go far to modify and, perhaps, arrest the progress of the later disease. Or, take cases of iritis; not in that the root of the iris blocks the ligamentum pectinatum or the spaces of Fontana, not that percolation

* Read before the Kansas City Ophthalmological Society, Kansas City, Miss., in March, 1937.

through the pupil is inhibited by the formation of synechiæ, but rather that an impaired circulation is brought about through changes in the aqueous, fibrin, pigment, leucocytes, all evidences of an associated pathological condition in the iris and ciliary body, and, taken separately or collectively, sufficient to alter the specific gravity of the aqueous itself, or, as individual elements, capable of blocking partially if not completely the delicate mesh work leading from the anterior chamber to the canal of Schlemm. Mackenzie was doubtless the first to apply surgical intervention with some intelligent idea (granted that such application, as many others, was empirical) for the relief of symptoms. For, granted also that in his day our means of diagnosis and our appreciation of iridocyclitis regarding its more or less elaborate classification had at this time not as yet arrived, yet in spite of this he anticipated a procedure which many of us even today are too prone to defer, if not to neglect, for a more refined, not to say, more difficult operative experiment; I mean paracentesis. For in the recognition of a rise in tension and the appreciation of the cause of such a rise two duties lie before us, neither of which can be followed as an alternative procedure. In the first place, one must release the intraocular tension by means of paracentesis, preferably well within corneal tissue, to be repeated at frequent intervals until such a time as normal intraocular tension is re-established; and, in the second place, the cause of the iridocyclitis, when once determined, must be treated energetically to a conclusion. The former procedure, namely, paracentesis, allows the pursuance of the second through the continued and energetic use of atropine and its allies. But of greater value even than this is the evacuation of a polluted aqueous of high specific gravity, filled with polymorphonuclear and other types of leucocytes as well as pigment cells and fibrin, constituting albuminous changes, retaining toxins, the by-products of the originally invading microorganism, the virulence of which is intensified relatively to the length of its incarceration. With such an evacuation come release in tension, reduction of œdema in the iris and ciliary body, especially as this applies to the blood supply, a vast army of reinforcements in the form of fresh leucocytes to take the part of those which have fallen in an unequal struggle, and, above all, a pure aqueous, possibly possess-

ing some bactericidal or antitoxic properties, but at least restored to its original physiological status as designed in Nature's course. I have already pointed out the rationale of such a procedure in my work on tuberculous iritis, and have asked if tuberculous peritonitis with complicating ascites can be successfully treated by laparotomy and irrigation, why should not tuberculous iritis be treated with a like degree of intelligence, more particularly in view of the fact that the result of treatment can be watched with greater accuracy.

The foregoing has been mentioned not so much as a surgical procedure as an appreciation of an established pathological fact, the logical treatment of which has to be undertaken and followed to a logical conclusion at all hazards, with surgery in this instance the handmaiden of medicine. A more remote effect of paracentesis I will refer to later.

It has been the usual practice to subdivide glaucoma into primary and secondary, congestive and non-congestive, inflammatory and simple, and other such subdivisions, and to apply various forms of surgical technique to fit the particular type. An argument as to which method is the best has arisen. The consequence of neglecting a careful analysis of the contributing factors underlying glaucoma is that a surgical procedure most excellent in one type of disease is blamed, and quite unworthily so, when it is applied in a condition for which it is not suited. Further, in a survey through any encyclopædia devoted to surgical procedure, I do not suppose that there is any one realm that offers more ways of doing the same thing than does glaucoma. A smoke screen of names in many cases has beclouded the issue, to say nothing regarding the situation which the modern ophthalmic surgeon must face if left alone with a series of names and his honest intention. When analyzed, these various procedures mean one thing only, the adoption of some surgical principle that will release the aqueous from the anterior chamber and restore intraocular equilibrium in so far as tension is concerned. It is consequently the concern of the ophthalmic pathologist not only to analyze this vast series, embodying very frequently most complicated methods of surgical technique, and, from an intimate knowledge of the tissue changes occurring in glaucoma, either to encourage or defer the adoption of certain positive surgical prin-

ciples, principles concerned with the elimination of pathological hindrances, as he can best interpret them.

Let us provisionally assume a very broad classification, embracing practically all forms of surgical endeavour. These fall under three heads, as follows: (1) reduction; (2) short circuiting; (3) radical. Under reduction are included paracentesis, iridectomy, and cyclo-dialysis. Under short circuiting is comprehended that vast series of operations devised to establish cystoid scars, iris-inclusion operations, and sub-conjunctival drainage. By radical I mean those unfortunate cases in which the ultimate health of the eye or of the individual is jeopardized, and where the removal of the organ is deemed the wiser course.

In my introductory remarks I mentioned the value in certain selected cases of corneal paracentesis. And at this juncture I would like to emphasize the inestimable assistance which in late years has been rendered ophthalmology by a knowledge of morbid histology and by an intelligent appreciation of the microscopy of the living eye made possible by the slit lamp. Subjective symptoms are frequently of value, but quite as often absolutely insidious and misleading in a relatively quiet eye. But now, how often is a diagnosis of glaucoma established, either with or in spite of those subjective symptoms, by the discovery of cells circulating in the aqueous, or, as I have noted in one case formerly under my care, of a solitary eyelitic dot on the back of the cornea.

Paracentesis may clear the channels of excretion of the various elements referred to above and assist in the elimination of the causes which produce them. There is a more remote possibility in that occasionally an accidental factor has to be reckoned with, of secondary assistance, through the establishment of a cystoid scar, brought about by the frequent opening of the original corneal incision and the establishment of a filtering cicatrix through the inclusion of a tag of Descemet's membrane, pigment cells, or a tiny knuckle of iris, or other such element.

It is unnecessary to do more than draw your attention to how manifestly unfair it would be to expect assistance through such an operation where anterior or posterior synechiae are involved, or where the spaces of Fontana are blocked by pigmentary changes, sclerosis of the fibres of the pectinate ligament, or by such a

possibly remote cause as thrombosis of one of the venae vorticosae. The operation is primarily of value in inflammatory conditions, whether recognized clinically as such or not. It is also a safe procedure in hæmorrhagic cases with marked hypertension until such a time as a lowered tension permits some more radical operation to be undertaken.

Under reduction would naturally fall the operation that has immortalized the name of von Graefe, a procedure which in properly selected cases has never been superseded by any other surgical endeavour in its efficiency in saving sight. Whether we accept the theory of Priestley Smith regarding the disproportion between the lens and cornea and the rest of the globe, that of Martin Fischer regarding œdema following colloid changes in the vitreous, or the more debatable one regarding the action of the fibres from the cervical sympathetic as vaso-dilators at the filtration angle, the result in all cases is identical. A dilatation of the veins invariably follows, a swelling or œdema of the iris, a falling forward of the root of the iris, and an ultimate occlusion of the filtration angle from œdema rather than from actual inflammatory changes. In such a condition there is an attendant apposition, but not necessarily an adhesion, of the root of the iris and that part of Descemet's membrane concerned in the formation of the pectinate ligament, if you will appreciate this subtle difference.

With the globe in a state of hypertension, such as is found in acute glaucoma, after excising the iris to its root a release from œdema must immediately follow. The apposed iris stump then falls back to its former normal position, to shrink into a more or less atrophied membrane, through the formation of terminal emboli where the blood vessels near the root of the iris have been severed. Provided that the iris stump is not included in the section, and in consequence permanently blocking off the angle, it is very unlikely that relapses will occur. It is needless for me to emphasize how guarded one should be in such cases of inflammatory or congestive glaucoma with underlying high blood pressure and arteriosclerotic changes. One naturally fears a hæmorrhagic tendency underlying the symptoms which may spell disaster through an expulsive hæmorrhage, if not anticipated. As a precautionary measure a posterior sclerotomy, or even a paracentesis, may

be attempted, until such a time as the acute inflammatory changes have subsided, the cornea cleared, hypertension released, and, possibly, an opportunity afforded the surgeon to view the fundus.

A class of case helped by iridectomy, not necessarily inflammatory or primary, is that of old established iritis which has passed the acute phase. Here the blocking at the filtration angle is established by synechiæ. Whether these be anterior or, as is more frequently the case, posterior, the circulation of the aqueous is cut off from the posterior to the anterior chamber and consequently to the filtration angle. It requires no stretch of imagination to understand how the excision of even a small sector of iris will release the complications thus involved. That the operation is absolutely unwarrantable in many cases should be acknowledged by any one possessing even the rudiments of pathological appreciation. Take two classes of cases, each apparently, at times, at least, non-inflammatory in its clinical appearance.

The first is one possessing a maintained shallow anterior chamber, the iris at the filtration angle, after a series of sub-acute attacks, not being acutely engorged and the eye consequently painful, but, from the repetition of attacks, the exudation of post-inflammatory lymph and leucocytes, an actual cohesion takes place between it and the back of the cornea in the region where Descemet's membrane breaks up to form the pectinate ligament. A series of plates taken from a section from such an eye in which an iridectomy had been unsuccessfully attempted, very kindly sent to me by my friend Sir John Parsons, shows how futile such an endeavour must be. To open up the spaces of Fontana or the canal of Schlemm in such a case is a technical impossibility, Jervoy's and, more recently, Otto Barkans's views to the contrary.

The second is illustrative of glaucomatous eyes possessing an apparently normal or possibly a deep anterior chamber. Such eyes may possess angles where the channels of excretion are in no way blocked by the root of the iris but by the elements of chronic degenerative processes as manifested by pigment in the spaces of Fontana, or even by sclerosis of the fibres of the pectinate ligament, as advanced by Thompson Henderson. An abscission of the iris in this as in the former parallel instance would be as unsuccessful as it is irrational.

De Wecker, von Graefe's favourite pupil, easily appreciated the shortcomings of iridectomy in chronic glaucoma, and attributed whatever success the operation held to some fortunate complicating feature about the incision. Czermak thought it almost impossible to establish by operative means an entirely new channel of exit in cases where the natural channels have been permanently closed. The reason of success in certain types of cases of iridectomy will be referred to when dealing with anterior sclerotomy.

Cyclodialysis is an operation regarding which I am not entitled to speak with any degree of authority, not having practised it, and not having seen it undertaken many times. The consensus, in referring to the literature, would seem to be that while for a time it may lower tension this effect is not permanent and that the operation is not equal either to iridectomy or to some of the more recent advances in ophthalmic surgery. Regarding the operation pathologically in chronic cases, it is difficult to see how the delicate spatula in the eye with a shallow chamber, after once separating or dislocating the ciliary body from the sclera, could penetrate through the dense connective-tissue elements established between the iris and the back of the cornea. Again, in the eye with the deep chamber it is equally logical to suppose that should the spatula reach the anterior chamber the same elements of degeneration or pigmentation, etc. would soon abolish this newly found avenue for an attempted escape of the aqueous.

By short circuiting I include practically every form of operation that is calculated to establish a cystoid cicatrix and one form or another of sub-conjunctival drainage. Their name is legion. Let us for a moment consider anterior sclerotomy, and here, too, may be included those cases where iridectomy has been performed and where success has not been attributed to the operation *per se*. The reason for success in these cases is perfectly logical, as many earlier writers, notably De Wecker, Czermak, and, later, Balantyne, have pointed out. For a cystoid sear may be established by a number of factors entering into one's operative technique, not necessarily by malice aforethought, as is frequently desired, but quite independently of any initiative on the part of the operator. For example, the inclusion of a section of Descemet's membrane within the lips of the wound is certainly

eyeballs in which the operation was performed, illustrating advanced glaucomatous processes of directly opposite types, but each absolutely opposed both to any theory or practice that the operation might pretend to support.

One word in conclusion regarding the so-called absolute glaucoma where radical measures have to be adopted. It is quite unnecessary for me to acquaint you with the cause of absolute secondary glaucoma. Haemorrhage, retinal detachment, thrombosis, ruptured vitreous, tumours, all spell blindness and ultimately suffering. Conditions are oftentimes so marked from lenticular changes, haemorrhages in the vitreous, or, more likely, from corneal oedema, that intra-ocular tension cannot be detected, though possibly suspected. Such eyes, when

recording even a fragment of light, but with pain and faulty projection, are better in a bottle.

I have tried to make the exception in three cases of dislocated lenses which went on to an advanced glaucomatous condition associated with keratitis bullosa when trephining was resorted to. Two ultimately came to enucleation. In the first case the trephine hole was blocked by the iris which was pushed forward by the lens which occupied the anterior chamber. The second was unsuccessful because of the prolapse of the vitreous into the anterior chamber and against the root of the iris. The third case was operated upon by me in 1916, and when seen less than four months ago the patient was in absolute comfort and still in possession of his eye.

THE NEED FOR PROLONGED ARTIFICIAL RESPIRATION IN DROWNING, ASPHYXIATION AND ELECTRIC SHOCK

By GORDON BATES, M.B., R. E. GABY, M.D., F.R.C.S.(C.) AND
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"The importance of getting to work with artificial respiration without a moment's delay has been emphasized by those who have had much experience in electrical accidents. No less important is the necessity for continuing artificial respiration until it is *certain* that death has occurred; nothing less than cooling of the body or the onset of rigor mortis should be considered to be evidence of death here." This most important statement appeared in the Goulstonian Lectures by A. J. Jex-Blake (*British Medical Journal*, March 8, 1913).

THERE are several widespread misconceptions concerning the possibility of resuscitation in cases of drowning. Most outstanding are these.

1. That immersion for more than four or five minutes is invariably fatal.

2. That in an apparently drowned person absence of the ordinary signs of life, notably pulse beat, respiration and audible heart sounds, means death, and that if these are absent artificial respiration is unnecessary.

3. That artificial respiration need only be kept up for a limited time, half an hour to an hour. As a matter of fact these ideas are all ill-founded. *It is possible for a person to have been under the water for up to half an hour and still live.* All signs of life may be absent in these cases even for hours. Life under these conditions may still be present, and the person may be revived. Artificial respiration should be

kept up for many hours in cases of apparent drowning, just as in the case of electrical shock, carbon monoxide poisoning, etc. The only really safe plan is to continue efforts until rigor mortis has set in.

In this connection it is interesting to note that in Reese's "Jurisprudence and Toxicology", printed over thirty years ago, the statement is made that a person may be under the water for fifteen minutes and still live, although in such cases the suggestion is made that there has been syncope.

With reference to drowning there are many stories of persons who have been submerged for long periods of time. In many cases exact records are not available. The following are of interest.

1. A doctor reports that in Newfoundland a man fell into the water and was submerged for half an hour. He was revived after prolonged artificial respiration.

2. A doctor in Ontario reports the case of a man who was under the water for from 20 to 30 minutes and was successfully revived.

3. The American Red Cross reports a case in which a man was in the water for 32 or 35 minutes and was revived by artificial respiration.

4. In June, 1938, a boy fell into the Kingston Harbour and was submerged for 9 minutes. He was successfully brought around by prolonged artificial respiration.

5. In June, 1938, a child fell into the water in Halifax. Newspaper reports stated that this child was revived after submersion for 10 minutes.

6. A doctor practising in Ontario near Lake Erie reports a case in which a boy sitting on a log fell into the water as the result of a swell from a passing speed-launch. This boy sank in deep water and his body was not recovered for 15 minutes. He was revived as a result of prolonged artificial respiration.

Experimental work on animals carried out by Dr. Ian Urquhart and, later, by Dr. G. H. Ettinger, and reported in the *Journal of Industrial Hygiene*, proved that the passage of an electrical current through an animal causes paralysis of the higher nervous centres, preventing normal reflex responses and hence preventing normal reflexes from various tests for death. An investigation into a considerable number of electrical shock cases by one of the present authors showed that where artificial respiration was started within one minute of the electrical shock, 90 per cent of the victims were resuscitated; where there was a delay of six minutes, only 10 per cent were resuscitated.

Experience has shown that what has been found in the case of electric shock can be applied to cases of drowning and of carbon monoxide poisoning. There is no doubt that many lives could be saved by the prompt application of artificial respiration by well trained persons, and the continuation of this artificial respiration until the patient breathes of his own volition or there are specific signs of death, such as the onset of rigor mortis.

Based upon the evidence that has been developed, a committee under the auspices of the Health League of Canada has been developed with the object of giving wide publicity to the benefits of artificial respiration, collecting field data in regard to drowning, electrical and gas poisoning cases, and carrying out physiological experiments on animals, with a view to perfecting these remedial measures.

In view of the fact that an electric shock accident is one of the most severe hazards in electrical public utilities for a number of years all employees of electrical public utilities in Canada have been thoroughly trained in artificial respiration by the standard technique, based upon the work of Sir Edward Sharpey-Schafer. This training has included a demonstration and explanation of artificial respiration, and the fieldmen of these utilities are required to practise artificial respiration at least once a month, acting as patient and as operator, during these practices. As a result of the training

so given many lives have been saved from electric shock, drowning and gas poisoning. The following are simply examples of case histories of these resuscitations.

CASE 1

On May 20, 1927, a young lineman came in contact with 26,000 volts at 2 o'clock in the afternoon. He was unconscious and not breathing. He was lowered to the ground and artificial respiration started by fellow employees; this was continued on the floor of the ambulance while he was being transported to hospital, also on boards on top of a cot at the hospital. Communication was established between the local doctor and consultants in a large city and it was not until 10 o'clock at night that the man was breathing by himself.

In this case it required 8 hours of artificial respiration until the man was safe. This is the longest case of resuscitation from electrical shock of which there is any record.

CASE 2

On May 21, 1926, a young man in carrying out cleaning in a power house, received a shock of 22,000 volts. In this remote power house fellow employees immediately started artificial respiration, and in about 45 minutes the man was breathing. His burns were so severe that he could not be moved and a doctor and nurses were brought to the point, where he was kept for four days. He was removed to a large city hospital where his injuries were found to be so severe that a large piece of his skull had to be removed. He has made a thorough recovery, and is carrying on a useful life with the same organization.

CASE 3

On July 7, 1937, a little girl was playing on a raft near a power house. She fell into the water and sank. Two boys swimming near the spot dived 17 times before they found the child on the bottom near the wall. She was brought to shore, artificial respiration started by a lineman, and after 35 minutes she was breathing normally but was unconscious. After 24 hours in the hospital she made a complete recovery.

CASE 4

On November 18, 1934, a young man was at his home and heard a commotion in a nearby house. On going in, it was found that the lady resident in the house had been overcome by gas. She was unconscious and not breathing. The young man had been trained by his father, and immediately started the application of artificial respiration; after a lapse of some time, and with the assistance of the father, natural breathing was restored and the woman made an uneventful recovery.

CASE 5

On March 18, 1936, a wife went out to the garage to see why her husband was delayed, and on opening the garage found him unconscious and not breathing and she screamed. Two young boys were in the next yard and went to find out what was the trouble. One was the son of a lineman and immediately pulled the man clear of the garage and started artificial respiration while the other boy went for help at the Fire Department and for a doctor. When this help arrived the young man had the patient breathing.

It is quite obvious that prolonged artificial respiration is applicable to all of the types of cases mentioned above. It is quite evident that if artificial respiration is started promptly by well trained personnel and continued without moving the patient, there is the greatest chance for the recovery of the patient. Much valuable

time is frequently lost by endeavouring to move a patient to a hospital, whereas if the artificial respiration were continued on the spot where the patient is, the patient could no doubt be revived and later taken to a hospital. The details of artificial respiration are shown in an appendix to this paper, prepared by the Electrical Employers Association of Ontario.

THE STANDARD METHOD OF RESUSCITATION

The following are the explicit instructions for carrying out the method by what is known as the standard technique:



Fig. 2.—Second position of operator giving artificial respiration.

Follow these instructions even if the victim appears dead.

ELECTRICAL SHOCK

Free the victim from the electrical contact as promptly as possible. Use a dry stick, dry rope, dry coat or other non-conductor. The use of your own hands without protection is dangerous and may add another victim to the accident.

GAS ASPHYXIATION

Remove the victim from the gas atmosphere into fresh air. Do not breathe the gas yourself even for a short time. If it does not overcome you it will cut down your strength.

DROWNING

Quickly remove the victim from the water and place on ground or other hard surface. Start artificial respiration at once.



Fig. 1.—Position in which patient should always be placed and kept until conscious, also first position for operator starting artificial respiration.

The pressure you must exert is the best means of forcing water out of the lungs and breathing passages. *Instantly attend to the victim's breathing.*

As soon as victim is clear rapidly feel with your finger in his mouth and throat and remove any foreign body (tobacco, false teeth, etc.). If mouth is tight shut pay no more attention to it until later. Do not stop to loosen patient's clothing, but immediately begin actual resuscitation. Every moment of delay is serious. Proceed as follows:

1. Lay the patient on his belly, one arm extended directly overhead, the other arm bent at elbow and with the face turned outward and resting on hand and forearm, so that the nose and mouth are free for breathing (see Fig. 1).

2. Kneel straddling the patient's thighs with your knees placed at such a distance from the hip bones as will allow you to assume the position shown in Fig. 1. Place the palms of the hands on the small of the back with fingers resting on the ribs, the little finger just touching the lowest rib with the thumb and fingers in a natural position, and the tips of the fingers just out of sight (see Fig. 1).



Fig. 3.—Third position of operator giving artificial respiration.

3. With arms held straight, swing forward slowly so that the weight of your body is gradually brought to bear upon the patient. The shoulder should be directly over the heel of the hand at the end of the forward swing (see Fig. 2). Do not bend your elbows. This operation should take about two seconds.

4. Now immediately swing backward so as to completely remove the pressure (see Fig. 3).

5. After two seconds swing forward again. Thus repeat deliberately twelve to fifteen times a minute the double movement of compression and release, a complete respiration in four or five seconds.

6. Continue artificial respiration without interruption until natural breathing is restored, if necessary, four hours or longer, or until a physician declares the patient is dead.

7. As soon as this artificial respiration has been started, and while it is being continued, an assistant should loosen any tight clothing about the patient's neck, chest or waist. **KEEP THE PATIENT WARM.** Do not give any liquids whatever by mouth until the patient is fully conscious.

8. To avoid strain on the heart when the patient revives he should be kept lying down and not allowed to stand or sit up. If the doctor has not arrived by the time the patient has revived he should be given some stimulant, such as one teaspoonful of aromatic spirits of ammonia in a small glass of water or a hot drink of coffee or tea, etc. The patient should be kept warm.

9. Resuscitation should be carried on at the nearest possible point to where the patient received his injuries. *He should not be moved from this point until he is breathing normally of his own volition, and then moved only in a lying position.* Should it be necessary, due to extreme weather conditions, etc., to move the patient before he is breathing normally, resuscitation should be carried on during the time that he is being moved.

10. A brief return of natural respiration is not a certain indication for stopping the resuscitation. Not infrequently the patient after a temporary recovery of respiration stops breathing again. The patient must be watched and if natural breathing stops artificial respiration should be resumed at once.

11. In carrying out resuscitation, it may be necessary to change the operator. This change must be made without losing the rhythm of respiration. By this procedure no confusion results at the time of change of operator and a regular rhythm is kept up.

If alone with the victim, do not neglect immediate and continued resuscitation in order to call a doctor. Start at once—the first few minutes are valuable. If other persons are present, send one of them for a doctor without a moment's delay.

The ordinary and general tests for death should not be accepted and any doctor should make several very careful and final examinations and be sure specific evidence is present before pronouncing the patient dead.

In view of the careful study and extensive experiments carried out under the late Professor MacLeod's direction this statement from him is extremely important.

"Paralysis of the nerve centre which controls breathing is the cause of death in many cases of electrocution and, provided the heart has not been directly affected by the current, natural breathing can often be restored by artificial respiration. This allows the still circulating blood to be aerated in the lungs. The only method to employ is Schafer's Prone Pressure Method and a pulmotor or any other form of apparatus should never be used. Since the paralysis of the breathing may last for some time it is necessary to continue artificial respiration sometimes for hours and it should never be discontinued until it is absolutely certain that the heart has ceased beating. As far as can be judged by observations on electrocuted animals, no advantage is gained by using oxygen or carbon dioxide during the artificial respiration, or by administering heart stimulants. It is important to see that the body is kept warm. After natural breathing returns the patient must be kept lying down and he must be carefully watched for several hours to see that the paralysis of breathing does not return. If it does so, artificial respiration must be reapplied."

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THE PERCUTANEOUS TUBERCULIN REACTION*

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THE only certain way of combating tuberculosis, with our present knowledge of the disease, is by early detection and careful supervision. Early detection implies discovery in childhood. The usual method of screening groups is by intradermal tuberculin testing (Mantoux). This test when properly performed by graded dosage is 100 per cent efficient.

Quite apart from the fact that some knowledge of technique is required for doing the intradermal test, this causes a slight amount of pain to the recipient. To an adult the intradermal test suggests no difficulty but to the

oft-pricked, pain-protected modern child with over-solicitous parents the thought of another injection is often sufficient to lose for the physician the chance of discovering an early case of tuberculosis. Add to this (a) the nuisance of sterilizing needles and syringes and obtaining standard dilutions of old tuberculin or purified protein derivative (P.P.D.) and (b) the well-recognized fact that early cases must often be detected by the general practitioner or public health nurse. Although these objections to the intradermal test may appear to be unimportant they are far from being so in practice and actually they have a serious detrimental result. It is obvious that tuberculin testing is not carried out with nearly sufficient frequency today.

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Arvid Wallgren¹, of Göteborg, Sweden, has accurately described "Initial fever in tuberculosis". He has found that, as a general rule, allergy is well marked when the fever is caused by the primary tuberculosis. For this reason he has encouraged the use of Hamburger's percutaneous ointment and over a period of years has enabled Swedish physicians and nurses to find many early cases of tuberculosis, with a subsequent and natural reduction of the disease.

In 1907 Moro and Doganoff² first described an inunction method for the diagnosis of tuberculosis. This ointment consisted of old tuberculin in a base of anhydrous wool fat. Hamburger³ introduced the so-called perkutan ointment, which consisted of old tuberculin evaporated to a constant weight. Lowenstein,⁴ Malmberg and Fromm,⁵ Wolff and Hurwitz,⁶ and others have also prepared slightly modified ointments.

During a visit to Sweden in the autumn of 1937, one of us obtained some of Hamburger's

culin. There were variations in their response to the injection of weaker solutions of the old tuberculin which are shown on an approximate percentage basis in Table II.

TABLE II. MANTOUX REACTIONS. SERIES OF 44 CASES.	
Old tuberculin intradermal	Positive reactions percentage
1-1,000	100
1-10,000	90
1-50,000	43
1-100,000	20
1-200,000	2

The ointment used in testing these patients was made by absorbing old tuberculin with Fuller's earth and then adding enough lanolin to make an ointment. On a quantitative basis, 1 c.c. of old tuberculin required 1 gram of Fuller's earth and 2.25 grams of lanolin. When 1 c.c. of old tuberculin was taken up with lanolin alone, 7.8 grams of lanolin were required. The ointment made with Fuller's earth was used for the testing, not that we know of any objection to an ointment with a plain lanolin base but merely because, being of a stronger concentration, it was presumed that it might act more effectively. No attempt was made in the course of this study to compare the relative efficiency of different strengths of ointment.

Prior to application of the ointment the skin of the selected site on the chest over the sternum was cleansed with ether, then a small portion of ointment (about the size of half a dry pea), was rubbed into an area about the size of a fifty cent piece. Holding a small bakelite ring on the skin with the other hand will aid in restricting the area of action if the rubbing is done inside it, but this is not at all necessary. As the amount of rubbing doubtless affects the result, sixty revolutions with the finger were taken as an arbitrary standard. A rubber finger cot was worn on the finger.

Within twelve hours, 73 per cent of the tuberculous cases showed pale or pinkish papules, either alone or with surrounding zones of erythema and the skin induration on the site of ointment application. After twenty-four hours there was a distinct reaction in 94 per cent and after forty-eight hours 100 per cent of the cases had reacted positively. Fig. 1 shows the percentage reaction after various lengths of time. It is interesting to note that 79 per cent of the cases still showed a reaction after one

TABLE I. NATURE OF TUBERCULOUS LESION IN 44 CASES. (Ages 23 months to 13 years).	
	Percentage
Parenchymal lesion	9.0
Combined parenchymal and tracheobronchial lymph node lesion.....	52.3
(a) With calcification	6.8
(b) With bronchiectasis	4.6
(c) With tuberculous osteomyelitis	2.3
(d) With tuberculous pneumonia	2.3
Tuberculous pleurisy with effusion.....	13.7
No demonstrable infiltration or calcification.	
Positive Mantoux	9.0

ointment, and on return to Canada commenced to test this ointment on known tuberculous children. The results were so encouraging that we decided to prepare an ointment and test it against graded intradermal reactions in known cases of tuberculosis.

The group that was studied intensively consisted of 44 cases. The patients ranged in age from 23 months to 13 years. The majority had either parenchymal or combined parenchymal and tracheobronchial lymph node lesions; there were also cases of tuberculous pleurisy and others who showed no demonstrable lesion but were positive tuberculin reactors. The approximate percentage composition of the group is shown in Table I.

All children in the group studied reacted positively to the intradermal injection of 1/10 mg. (1/10 c.c. of 1-1,000 solution) of old tuber-

week. In a few cases the skin reaction was discernible after seventeen days, when both papules and intervening skin had assumed a slightly brownish hue.

The papules, which are a distinctive feature of the skin reaction, varied in number from ten or twelve to more than one hundred in different cases. They are easily seen and felt. They did not appear to cause the patients any discomfort whatsoever.

In a general way, those patients who were known to be most allergic from their intradermal tests gave the most marked percutaneous reactions but there were enough exceptions to render

tubereulin was also used on all the patients tested in the general medical wards, to investigate the possibility of false positive reactions based on idiosyncrasy. Two patients with negative Mantoux reactions showed small areas of slight erythema on both test and control sites. These disappeared after 36 hours. No papules which seem to be the distinctive feature of the positive reaction were present. This transitory erythema without papules is presumed to have been a friction effect.

In conclusion the statement seems warranted that in a small series of carefully studied cases, results with our ointment have been consistently

PERCUTANEOUS TUBERCULIN REACTIONS				
SKIN REACTION	AFTER 12 HOURS	AFTER 24 HOURS	AFTER 48 HOURS	AFTER ONE WEEK
NO REACTION	27%	6%		21%
PALE OR PINKISH PAPULES	39%	59%	45%	62%
PAPULES WITH SURROUNDING ZONES OF ERYTHEMA. SKIN INDURATION.	23%	42%	41%	12%
PAPULES, CONFLUENT ERYTHEMA AND SKIN INDURATION	11%	13%	14%	5%
CHILDREN'S MEMORIAL HOSPITAL MONTREAL Series of 44 cases of tuberculosis			After 48 hours 100% of cases in this series gave a positive reaction to Tuberculin Ointment.	

Fig. 1

this impression tentative only. The really important finding was a definite papular reaction in all patients who reacted positively to the intradermal test with 1/10 mg. of old tuberculin.

After completing this somewhat intensive study on the patients in one of the tuberculosis wards, it was thought advisable to check the percutaneous test in the general medical wards. All patients there receive a Mantoux test as part of their routine investigation. A positive percutaneous reaction was obtained in the case of only three patients, which coincided exactly with the findings on routine intradermal injection of 1/10 mg. of old tuberculin. A total of 57 patients was examined in this manner. In age the patients varied from 2 years to 11 years. They were about equally divided as to sex, and suffered from a variety of diseases which are not pertinent to our study.

A control ointment containing the same amount of Fuller's earth and lanolin but no old

satisfactory. The cheapness of ointment testing, together with its stability, warrants more intensive application of the percutaneous test by physicians and others interested in detecting early cases of tuberculosis in childhood.

In our hands, and with the cases tested, the percutaneous test has been as reliable as the intradermal injection of 1/10 mg. of old tuberculin. It is not suggested however, that this ointment should take the place of the various dilutions of old tuberculin or purified protein derivative used in hospital practice. It is as a *case-finder outside hospitals* that we believe that tubereulin ointment has a definite field of usefulness. It should enable us to discover many more cases of childhood tuberculosis than are brought to light at the present time. Carried in one's bag, tubereulin ointment is instantly available and readily applicable in many situations where a syringe and needle are not, or where the environmental situation militates

against their use. Whenever possible the intradermal test is the method of choice but in the numerous situations in which it is not being applied today, for one reason or another, we feel that the percutaneous test has much to recommend it in the interests of public health.

SUMMARY

An ointment which may be used as a skin test in tuberculosis case-finding is described. It was compared with the intradermal tuberculin test in 44 cases of tuberculosis and 57 general medical cases with very favourable results. The use-

fulness of this ointment for the detection of early cases of tuberculosis on a wider scale is discussed.

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CARDIAC LESIONS IN ADRENAL INSUFFICIENCY

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FOR several years one of the authors (C.¹) has been conducting studies* on experimental adrenal insufficiency in relation to Addison's disease, with particular reference to the preparation of extracts of adrenal cortex and the assay of cortical extract on various species of experimental animals (Cleghorn *et al.*^{2,3}). More recently this author and his collaborators have reported on the vascular failure in adrenal insufficiency (Armstrong *et al.*⁴) and submitted evidence that this is due at least in part to the inability of sympathetic nerves to elicit their usual effect. It was suggested that this might be due to depletion of the so-called "ad-substance", the adrenalin-like mediator of sympathetic nerve impulses. The other author (H.) became interested in the present problem from another angle—that of producing an imbalance of the autonomic nervous system.

The original hypothesis of Hall and Banting (1930), which postulated that organic effects of physiological dysfunction occur in one or more local areas as a result of an autonomic imbalance produced by persistent overaction of the parasympathetic has received substantial support from the experiments of several other workers. Informal discussions between the authors of the present paper eventually resulted

in the decision to collaborate in the further investigation of the field involving autonomic imbalance by the suppression of sympathetic effects by adrenalectomy.

It has been recorded by Banting and Gairns⁶ and others that duodenal and gastric ulcerations with hæmatemesis, melæna, etc., commonly occur in adrenalectomized dogs. In view of the sympathetic failure in adrenal insufficiency described first by Elliott,⁷ and more recently investigated by Cleghorn and his collaborators, this might be considered a parasympathetic effect, resembling as it does so closely the lesions observed by Hall, Ettinger and Banting.⁸ If this were so it might be expected that cardiac changes as found by these authors might be met in animals dying of adrenal insufficiency. No reference has been found, however, describing the occurrence, or even intimating the possibility, of cardiac lesions, and few referring to cardiac dysfunction in experimental adrenal insufficiency. The present paper deals with this phase of the problem.

Although many publications have appeared and much experimental work has been presented on the clinical behaviour of dogs in acute and chronic adrenal insufficiency and their response to cortical extract and high salt diets, etc., only a very few of these have included, even in their protocols, any reference to the cardiovascular system. Rogoff and

* The extract used in these experiments was made under the direction of Dr. E. W. McHenry in the Connaught Laboratories (Cleghorn, McHenry, McVicar and Overund⁵) and obtained through the kindness of Prof. C. H. Best and Dr. McHenry.

Stewart⁹ noted a slowing of the heart-rate in adrenalectomized dogs in the terminal stages of adrenal insufficiency. Harrop *et al.*¹⁰ and Swingle *et al.*¹¹ have likewise mentioned a bradycardia under similar conditions. This slowing of the heart was believed by Nicholson and Soffer¹² to be due to a change of the "plasma electrolyte pattern", a result of the increase in potassium content of the blood. Their electrocardiographic records showed an absence of P waves and were presented as evidence of auricular fibrillation.

Observation of this marked bradycardia in terminal insufficiency prompted a closer examination of the heart of these animals which revealed definite cardiac lesions. This finding which, so far as we are aware, has not been previously described was reported on in brief by Banting and Hall¹³ and by Hall and Clegghorn,¹⁴ who showed electrocardiographic and kymographic evidence of marked cardiac dysfunction as a result of adrenal insufficiency. These experiments were begun in 1935 and now include a large series of dogs. Recently Nilson,¹⁵ while commenting on the mineral metabolism of adrenalectomized dogs, mentioned that his dog had a depressed heart beat and that "fatal insufficiency is characterized by cardiac failure". Nilson himself may have attached some significance to this observation but in his paper the finding is recorded without further comment.

EXPERIMENTAL

The animals (dogs) used in these experiments were bilaterally adrenalectomized in two stages. Post-operative treatment included intravenous normal saline and cortical extract, followed by subcutaneous injections of the hormone twice daily until the animal was gaining weight and otherwise in excellent health. At this time a series of normal electrocardiograms was taken and estimations of blood non-protein nitrogen, Na and K were made. Hematocrit determinations were also recorded. The administration of cortical extract was then discontinued. During the period of insufficiency routine examinations of blood were made; electrocardiograms were taken with increasing frequency as the clinical condition of the animals became progressively more grave. From our work only a few typical experiments will be presented.

In a typical experiment one dog (D 18) was adrenalectomized and extract given for 9 days, at which time, the animal being in excellent condition, extract was discontinued. Electrocardiograms taken at that time showed no change from the normal

(T_I-ve, T_{II}-ve and T_{III}-diphasic).*

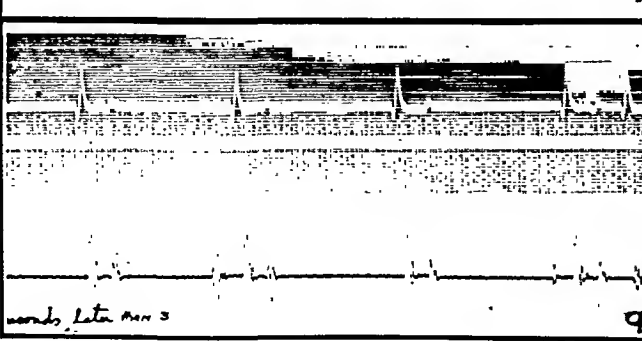
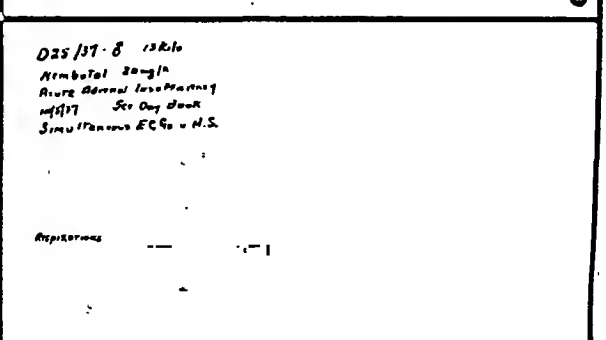
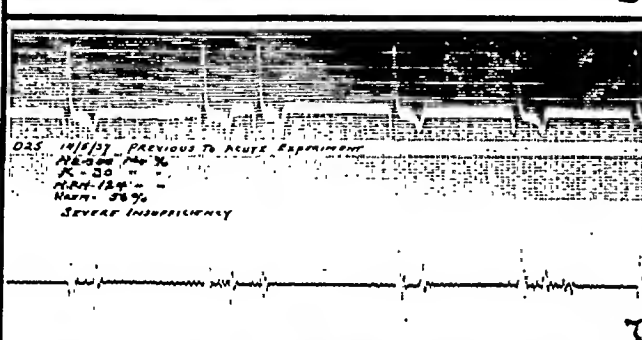
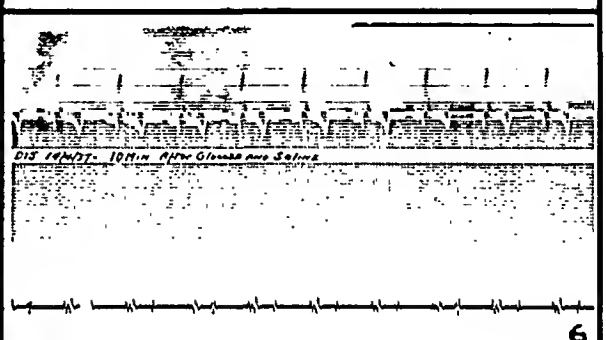
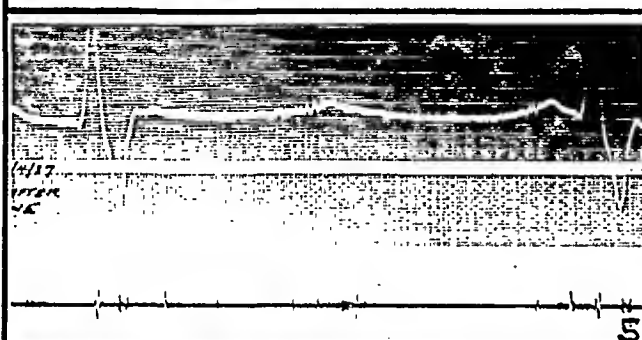
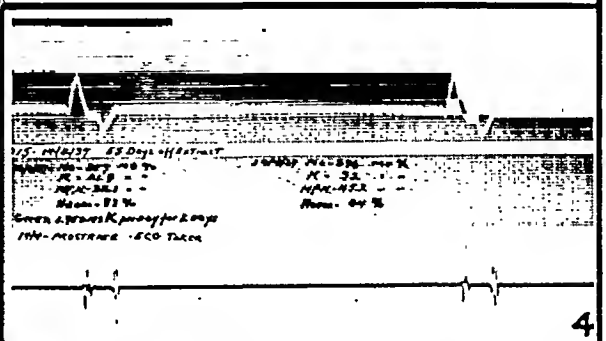
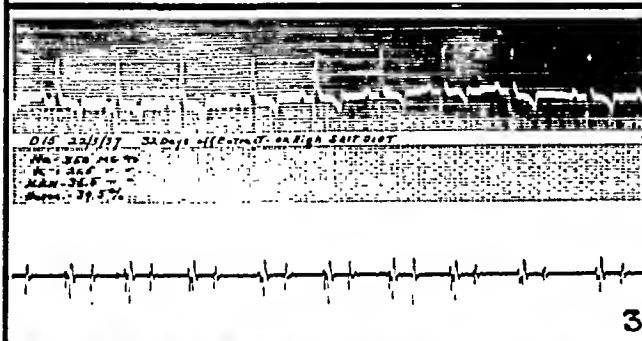
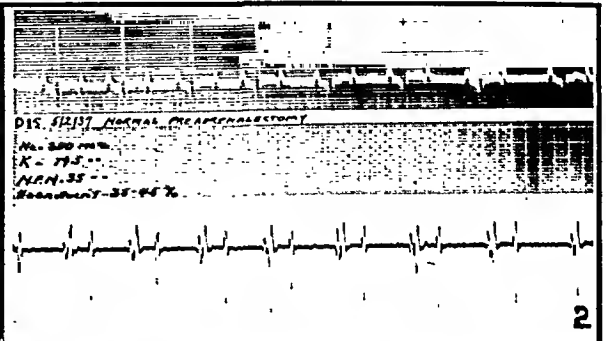
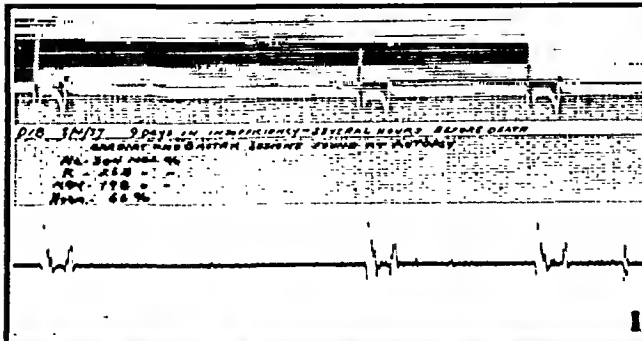
The heart-rate was 110 to 120 per minute. Within 8 days the heart-rate had decreased to 90, and as the dog developed definite clinical signs of insufficiency the heart-rate suddenly decreased to 36 per minute. Atropine did not change the heart-rate. Electrocardiograms taken at this time showed very slow irregular ventricular complexes with a complete absence of P waves. In lead I the R waves were of extremely low voltage. T_I had become definitely positive, T_{II} diphasic and T_{III} more negative.

An irregular type of heart block, 4:1, 2:1, 3:1, etc., was evident throughout the electrocardiograms, as the following electrocardiogram (lead II) shows (Fig. 1). Note also the low voltage slow waves to be seen between the apparent ventricular complexes. It will be noted that the simultaneous heart-sound record shows the presence of a systolic murmur. Single heart sounds are recorded without ventricular complexes being apparent.

The changes in the composition of the blood were as follows: non-protein nitrogen from a normal of 45 up to 178 mg. per cent; K from 19.20 to 30.8 mg. per cent; Na from 350 mg. per cent down to 304; and the hematocrit reading had increased from 35.40 to 66 per cent cells.

The normal electrocardiogram of another dog (D 15) is shown in Fig. 2, together with its normal blood chemistry. Following a double adrenalectomy cortical extract was administered for 12 days, after which time the dog was maintained on a high salt diet without extract. Fig. 3 shows the electrocardiogram and blood chemistry after 32 days off extract on a high salt diet. The blood K, etc., are within normal limits. The electrocardiogram and heart-rate have remained normal. After 52 days on the salt diet, at which time the blood chemistry and electrocardiograms were still normal, the dog received 1.75 grams K (per os) per day for two days. The following day the animal be-

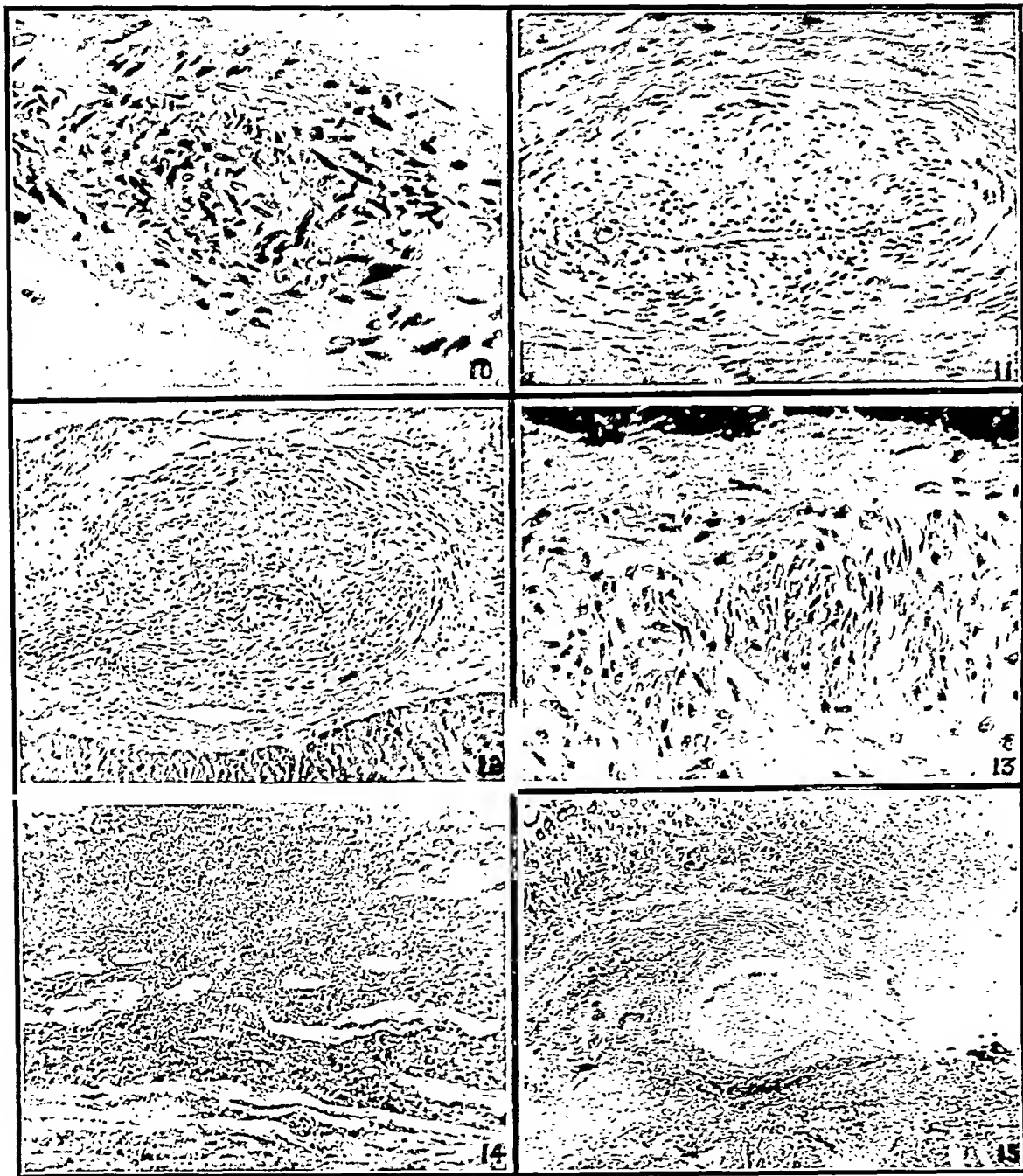
* In the dog the normal T wave may be positive, negative, or diphasic.



came prostrate, the blood K had increased to 32 mg. per cent, and the hæmatocrit reading to 44 per cent cells. The heart-rate decreased very rapidly to 30 per minute, and the electrocardiogram showed a ventricular complex indicative of marked myocardial ischæmia (Fig. 4). P waves were again absent.

Atropine (0.2 mg./kilo) produced only a very slight increase in heart-rate (from 30 to 44) but markedly increased the pulse pressure. The electrocardiogram (Fig. 5) showed a very

great increase in the voltage of both R and T waves with a continuance of the heart block. Short runs of auricular f waves and occasional P waves were also evident. Heart sounds appeared irregularly spaced within the cardiac cycle, duplications occurred, and systolic and diastolic murmurs were recorded. Within a few minutes, however, the ventricular complexes became more normal and f waves of auricular fibrillation were apparent. Heart sounds remained irregularly spaced, many appearing



during ventricular diastole. At this point the animal was given 30 c.c. cortical extract (intravenously in 3 doses at half hour intervals). The apex rate remained slow and did not exceed 53 beats per minute over a 3 hour period. When, however, 100 c.c. normal saline with 25 g. glucose were administered intravenously a very striking change was produced. Within a few minutes the animal revived from a most lethargic state to a fairly normal condition. The apex rate increased to 150 to 160 per minute, and the electrocardiogram showed a return of normal auricular complexes, normal voltage of R and T waves, and normal heart sounds (Fig. 6).

Some of the other dogs in insufficiency responded similarly to D 15. With exercise there was sometimes a very transitory increase in heart-rate from 40 to 50 up to 130 to 150 per minute; in some cases atropine did produce cardiac acceleration, which was not maintained. In normal animals atropine (0.2 mg./kilo.) will double or triple the resting heart-rate and maintain the increase for 30 to 45 minutes (Hall and Manning). In the "insufficient" dogs the atropine infrequently produced an acceleration which only lasted 3 to 5 minutes, after which time the rate would decrease very suddenly to its original slow rate of 35 to 45 per minute. The bradycardia in these dogs was accompanied by a low blood pressure of 40 to 60 mm. Hg. (direct femoral). When the animal has been maintained on a high salt diet the heart-rate and electrocardiogram remain normal and the effect of atropine is as pronounced as in the normal.

Fig. 7 shows the electrocardiogram of another dog (D C 25) in severe adrenal insufficiency. The P waves were entirely absent but no f waves were evident. (Note heart sounds). The apex rate was 52 per minute, the blood K 30 mg. per cent, non-protein nitrogen 124, and the hæmatoerit reading had increased to 56 per cent cells.

As in the case of most of the other dogs in this condition, this animal was anæsthetized (nembutal 20 mg./kilo.) and connected to a kymographic hook-up. In most cases there was an increase in heart-rate following the anæsthesia, but very frequently the heart spontaneously assumed its former slow rate. The injection of 0.05 mg. of adrenalin usually produced an increase in blood pressure of from 50 to 60 mm. Hg. As the blood pressure

reached its peak the pulse pressure also increased, and as the pressure declined, which required some 2 to 3 minutes, very marked pulse deficit occurred. Fig. 8 shows such a record; the irregularities in output are best seen in the tonometer tracing, but can also be seen in the manometer record. Simultaneous electrocardiograms and heart sound records were taken at the times indicated in the kymograph figure.

Electrocardiographically, no changes in heart-rate were noted immediately following the injection of adrenalin, but very marked irregularities in the R wave voltage were found. No three consecutive R's were of the same voltage, and in the electrocardiogram, marked 4 on the kymographic tracing Fig. 8, gross irregularities in the form of the ventricular waves had appeared. This complex now resembled a diphasic electrical potential wave, the R voltage having gradually increased from 2.0 to 2.7 milli-volts and the Q R S interval increased from 0.06 to 0.18 seconds. The heart-rate had decreased from 70 to 30 beats per minute. It is interesting to note that during the period of adrenalin hypertension additional heart sounds, divorced from ventricular complexes, were frequently recorded. These can be observed in Fig. 9. All of the other experimental animals in these groups showed electrocardiographic and clinical evidence of disturbed cardiac function with diminished or abnormal responses to exercise, drugs, etc.

Periodically throughout the stage of "insufficiency" evidence of dyspnoea and distress was noticed. Frequently, too, coarse râles were heard following such a bout of distress. This pulmonary oedema was usually evident at autopsy. The previously mentioned extrasystoles, irregularity of apex beat, changing T waves, extreme bradycardia, followed by a marked pulse deficit and, at times, associated with the complete absence of P waves indicated a definite cardiac dysfunction.

Terminally, these animals in chronic adrenal insufficiency passed tarry or blood-stained stools, frequently vomited "coffee-ground" material, lost their appetite, failed to maintain their weight and gradually became prostrate. Coincident with this state the blood K increased to 26 to 35 mg. per cent, the non-protein nitrogen to 50 to 180 mg. per cent and the hæmatoerit reading increased to 55 to 66 per cent cells.

AUTOPSY FINDINGS

Complete autopsies were performed on all animals. A general summary of findings only will be given.

Thorax.—The lungs as a rule appeared heavy, oedematous and congested. On opening the pericardium the right heart was dilated, the whole organ being soft and flaccid. Fairly discrete areas of congestion or pale infarcted areas were observed. Small areas of subendocardial hæmorrhage were sometimes noted, and in two instances marked circumscribed subepicardial hæmorrhage was found.

Abdomen.—The contents of the stomach and intestines were almost invariably blood stained. On the mucosal surface of the stomach a variable number of congested areas, many with punched-out ulcerated centres, were found. These ulcerative areas were most frequently found in the pre-pyloric portion, although the mucosa throughout the body of the stomach appeared unhealthy and lacked its usual tone and colour. Frequently, but not invariably, circumscribed areas of severe congestion and hæmorrhage were seen in the duodenum. A milder type of patchy congestion was evident towards the lower end of the ileum and again in the lower rectum.

The liver appeared slightly congested and in some cases mottling was seen.

In many cases the lymphoid tissue showed an hypertrophied condition. This finding confirms a previous report by Banting and Gairns.⁶

Other organs appeared normal.

Histological findings.—The heart sections showed many changes, mostly in the medium-sized and smaller arteries. In many instances the endothelial lining of the arteries was broken and in some cases almost completely absent. These endothelial cells were readily seen in the lumen of the vessels scattered amongst the blood cells (Fig. 10). In some sections recent thrombus formation was observed with its attachment to the vessel wall at the site of a break in the continuity of the endothelial lining. Other sections showed arteries whose walls were markedly oedematous and in some cases arterial spasm was evident (Fig. 11). Complete thrombosis of a number of medium-sized coronary arteries was also noted, and in some cases (Fig. 12) organization and recanalization of the thrombus had taken place. In two cases degeneration of the media of larger-sized coronary arteries was observed. In the one case illustrated (Fig. 13) the muscle cells of the media appear atrophic and degenerated, the nuclei stained poorly, and the cytoplasm of the remaining cells was definitely pink-staining.

In a great number of heart sections marked capillary congestion was seen. This congestion was not uniform throughout the sections from one heart nor uniform throughout any one section. It was associated with those dark spotty areas in the heart which upon gross examination gave evidence of congestion. Usually in the microscopic sections through these areas there was an associated unevenness in the staining of the myocardium. This was suggestive of early myocardial degeneration, although the nuclei of the muscle cells in these regions appeared normal. The degree of congestion in different hearts and in different sections varied a great deal, while in one heart marked hæmorrhage had occurred (Fig. 14).

Sections through congested areas in the stomach and duodenum showed varying degrees of congestion and degeneration. In many different sections the submucosal vessels were filled with red blood cells, and the capillaries extending into the villi were similarly dilated. In a large number of sections diapedesis or rhexis had taken place as blood cells were found in the lumen and on the mucosal surface. Other sections taken through ulcerated areas showed microscopic evidence of the ulcerative process (Fig. 15). Other sections taken through normal looking areas of mucosa appeared quite normal on microscopic examination.

Other organs.—Sections of the liver showed evidence of capillary congestion. In some cases the congestion

was widespread and quite marked, the more so in those cases where pulmonary congestion and oedema was marked.

The lung sections showed varying degrees of congestion but no consolidation nor pneumonia. The alveoli in some cases were filled with uniformly pale-staining material suggestive of a transudate. Capillary congestion was also noticed in a few kidney sections, although most of these sections from kidney appeared quite normal.

Microscopically, all other tissues appeared normal, although it was extremely difficult to interpret some of the sections of thyroid gland.

DISCUSSION

The interpretation of progressive electrocardiographic records, the analysis of results of acute experimentation, and the study of the microscopic sections of the animals used in these experiments supply evidence to show the importance of a normal functional equilibrium between the two divisions of the autonomic nervous system. Normally, the functional tone of the visceral organs, blood vessels, etc., is maintained, at least in part, by the balanced action of sympathetic and parasympathetic nerve function. This is effected by the local production at all nerve endings of the latter system of acetylcholine, and at most of the nerve endings of the former of an adrenalin-like substance (ad-substance). A few fibres of the sympathetic do release acetylcholine, but for the purpose of the present discussion may be neglected. Hall, Ettinger and Banting¹⁶ found that when the functional equilibrium is disturbed by increasing the acetylcholine in the body myocardial and gastro-intestinal lesions are produced. The results reported in this paper indicate that similar physiological and pathological changes occur when parasympathetic preponderance occurs as a result of a decrease in effective ad-substance in the body.

While complete adrenalectomy deprives the animals of the adrenalin-secreting medulla, this is not in itself a serious matter, since injection of an extract of the adrenal cortex permits the maintenance of the animal in apparently normal health. Obviously, then, the cortical extract supplies something to the body which in its absence leads to acute adrenal insufficiency and death. In addition to the maintenance of life the cortical extract also preserves in the adrenalectomized dog a substantially normal reactivity and responsiveness of the vascular bed to drugs and electrical stimulation of nerves, presumably through its direct effect upon the functional capacity of the ad-substance in the vascular system (Armstrong *et al.*⁴).

As an animal is allowed to go into adrenal insufficiency by withholding cortical extract the electrocardiogram shows changing ventricular and auricular complexes. The first evidence of cardiac disturbance is the change to an irregular heart beat, which is almost always followed by a sudden bradycardia. We would suggest that this bradycardia is at least partly the result of vagus preponderance and would indicate that at this stage of adrenal insufficiency the ad-substance was either depleted or ineffective. The innervation of the coronary arteries is chiefly vagal, although the larger branches are dually innervated by sympathetic and parasympathetic. Consequently, in adrenal insufficiency, when the mediator of sympathetic nerve impulses (ad-substance) is either exhausted or ineffective, control through the sympathetic fails, spasm of coronary arteries readily takes place and may be permanent, as was shown in Fig. 11. Thus the coronary blood flow is markedly decreased and evidence of cardiac ischæmia is manifested clinically as well as in the electrocardiographic records.

During the progressive stages of acute adrenal insufficiency the response of the heart to intravenously injected atropine changes. As mentioned previously, atropinization in the normal dog produces a very marked acceleration of the heart. In the early stages of adrenal insufficiency the heart still responds to atropine, but as insufficiency progresses to the stage of prostration the heart no longer accelerates following atropinization. This would indicate the inability of the sympathetic nervous system, through the exhaustion of ad-substance, to assume control following the removal of vagal effects by atropine. At this stage of insufficiency, vagotomy also fails to induce acceleration of the heart.

That the apparent exhaustion or ineffectiveness of the ad-substance is not complete nor permanent is indicated by the fact that even in the presence of severe insufficiency with prostration, where the electrocardiogram shows evidence of marked myocardial ischæmia with auricular fibrillation or heart block, the heart may be restored to normal rhythm by the intravenous injection of hypertonic glucose and saline (Fig. 6) or by the injection of adrenal cortical extract or both. These injections may, of course, exert their effect by withdrawing potassium from within the cells. However, from acute experiments, in which large

amounts of potassium were injected intravenously, it does not seem likely that the withdrawal of potassium from the cells is entirely responsible for the return of normal cardiac rhythm, nor, conversely, is the high potassium solely responsible for the bradycardia. For example, in a dog injected with potassium the level of this ion in the blood was raised from the normal of 20 mg. per cent to 30 to 40 mg. per cent without any effect on cardiac rhythm. This is the usual range of potassium values in severe insufficiency. It was not until the blood potassium values had been increased to 50 to 60 mg. per cent that cardiovascular effects were evident.

The rôle which the adrenal cortical hormone plays in the maintenance of adequate and effective ad-substance in the absence of the adrenalin producing adrenal medulla is the subject of further studies by the authors. It is not clear whether the cortex or cortical extract supplies a substance, (not adrenalin) which is necessary to render the ad-substance functionally active. It may be that in adrenal insufficiency the ad-substance does not become depleted or actually exhausted but that it becomes gradually more ineffective, either due to a precursor becoming exhausted or a physico-chemical change taking place at the adrenergic nerve endings. When either of these hypothetical mechanisms is adjusted by the administration of cortical extract, etc., the ad-substance once more becomes effective. The ineffectiveness of the ad-substance in insufficiency may be due entirely to a change in the permeability of the cells, and when the electrolyte pattern (ionic ratios) of the blood is rendered normal again the effectiveness of the ad-substance is again evident.

SUMMARY

1. Myocardial and coronary artery damage has been described in dogs dying of adrenal insufficiency.

2. Gastric and duodenal congestion and ulceration have been produced by the same mechanism.

3. It is suggested that these lesions may be the result, at least in part, of the relative over-activity of the parasympathetic nervous system when the sympathetic nervous system has been rendered functionally inactive following the development of experimental adrenal cortical insufficiency.

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THE RELATION OF PREGNANCY TO BILIARY DISEASE AND THE CONTROL OF THE VOMITING OF PREGNANCY*

BY JOHN M. MCGOWAN, M.D. AND J. O. BAKER, M.D.

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IT seems to us to be a fairly prevalent medical belief that pregnancy predisposes to disease of the gall bladder. In previous reports^{2, 4, 5, 7} it was shown that spasm of the muscle in the second portion of the duodenum closed the lower end of the common bile duct. Such a spasm could be produced at will in normal human subjects by subcutaneous injection of morphine, gr. 1/6 (Fig. 1). This duodenal spasm could be promptly and completely relieved by inhalation of amyl nitrite and partially relieved by sublingual administration of glyceryl trinitrate (nitroglycerin). In a few of the normal subjects studied morphine produced intense nausea and vomiting. This suggested to us that the predisposition to biliary disease and the nausea and vomiting of pregnancy might sometimes be due to a similar mechanism as that set up by morphine, namely spasm of the second portion of the duodenum.

VOMITING OF PREGNANCY

Recently we administered glyceryl trinitrate to a patient suffering from intractable vomiting of pregnancy with beginning jaundice, with the result that vomiting subsided after two days and a therapeutic abortion was avoided. Subsequent x-ray studies made by a special technique described elsewhere,¹ demonstrated the presence of a spasm in the second portion of the duodenum and relaxation of this spasm by inhalation of amyl nitrite (Fig. 2). We have reported a series of 12 cases of patients in whom glyceryl trinitrate had been administered for vomiting of pregnancy with consistently

good results. Five of these were patients in whom other methods of treatment had failed. Since reporting this series we have treated as many more patients with continued good results.

The method of administering the drug is as follows; we instruct the patient to take glyceryl trinitrate gr. 1/100 under the tongue after each meal. Because of the slight drop in blood pressure produced by the drug we advise the patient to remain in the lying position for 10 minutes after administration. The patients are encouraged to eat a full mixed diet. As we have found an extreme variability in the potency of the tablet triturates we prescribe the hypodermic tablets. The drug is considered potent if it produces flushing of the face after about three minutes. We warn the patients of the presence of a transient headache or a pounding sensation in the head which is occasionally alarming or leads to cessation of proper use of the drug. Vomiting usually clears up after three days' treatment. As to the number of tablets a patient can take a day, we have had one case, non-pregnant, of severe biliary colic with vomiting in which a dozen tablets each of a dose of gr. 1/100 were taken in 24 hours without any harmful results.

This treatment differs from other types of therapy which have been used for the control of the vomiting of pregnancy in that it has roentgenological evidence to show why it should be successful. In addition it has given good results in the case of patients who were treated in their own homes.

It is probable that glyceryl trinitrate will not be found successful in the control of vomit-

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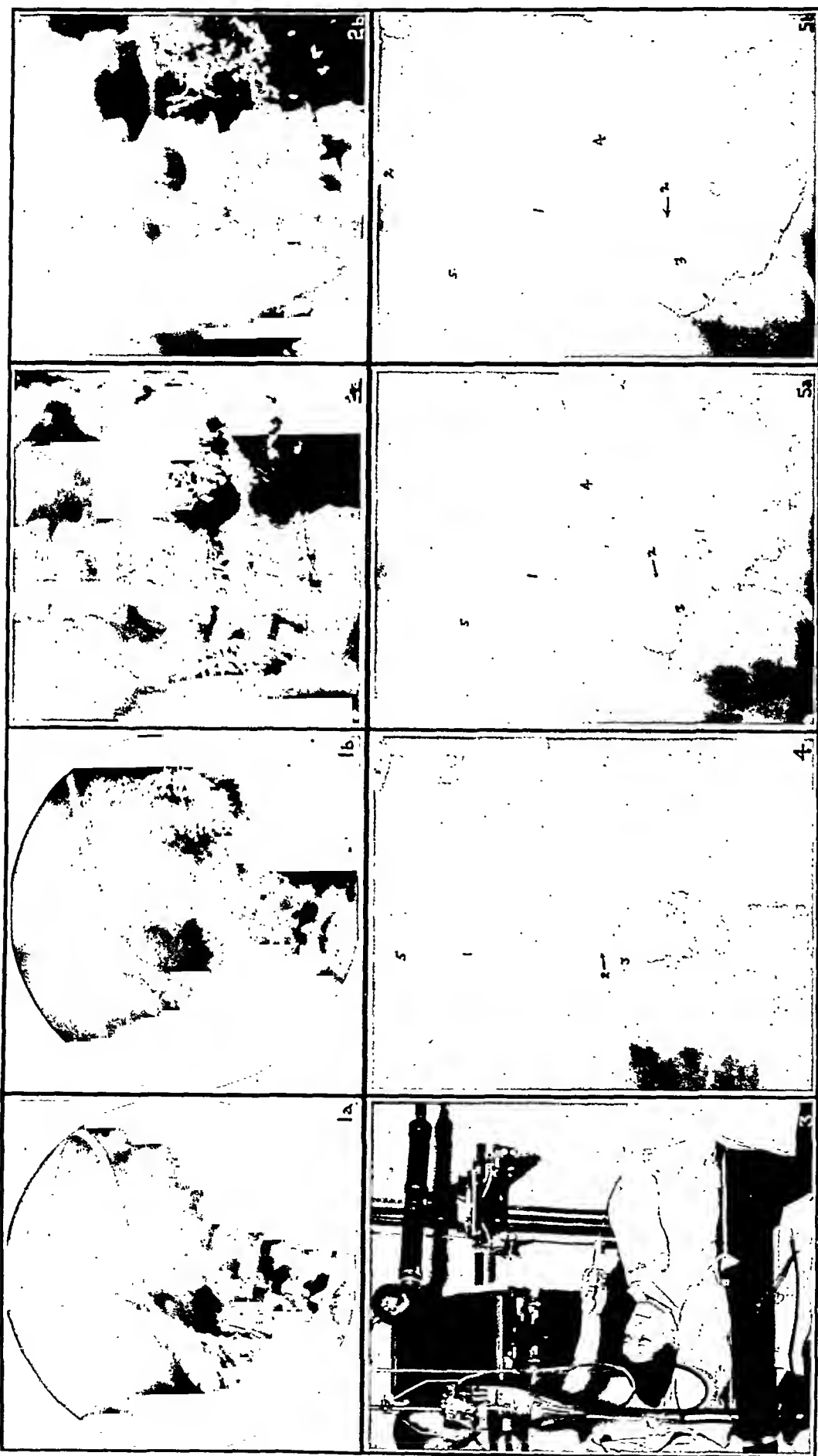


Fig. 1.—Normal duodenum following injection of the duodenum with barium. (a) Resting; (b) 10 minutes after injection of morphine. Note spasm of duodenum. Fig. 2.—Duodenum of a pregnant woman suffering from vomiting. (a) Showing spasm of the duodenum, second portion. No lumen is visible. The barium has been forced between the rugae. (b) The same following inhalation of amyl nitrite. The duodenum is now completely relaxed. (From Baker, McGowan, Lees and Torrie). Fig. 3.—Apparatus for measuring intra-biliary pressure. The pressure apparatus has been disconnected and the T-tube is being injected with brominol for x-ray study. Fig. 4.—The common bile duct of a patient with intractable post-cholecystectomy colic. (1) T-tube in duct. (2) Narrowing of lower end of

common duct due to spasm or fibrosis or both. Dilated common duct above. (3) Barium in duodenum. (5) Reflux of barium into the dilated intra-hepatic ducts. Fig. 5.—Same case as that of Fig. 4. (a) Note (2) narrowing of lower end of common bile duct close to duodenum. (3) Spastic duodenum. Note absence of duodenal lumen. Some barium has been forced between the rugae. (4) Duodenal tube. (b) Following inhalation of amyl nitrite. The duodenal wall is relaxed and the lumen is filled with barium. Some narrowing still exists at the lower end of the common duct which is probably due to fibrosis. If the biliary obstruction were due to spasm it should have been relaxed by amyl nitrite.

ing of pregnancy in every case, as in some cases the spasm may be so severe that the drug will be ineffective. The question why the nitrite drugs should relax duodenal spasm demands further investigation. We have certain evidence pointing to a relationship to sugar metabolism, possibly an increase in the ability of the spastic muscle to utilize sugar in order to be restored to its normal state. Sprague⁶ has found a reduction in the blood sugar following administration of glyceryl trinitrate in six cases. Walters, McGowan, Knepper and Snell⁷ have produced data indicating a relaxing effect on the duodenal wall resulting from subcutaneous injections of 20 units of insulin. We merely mention these findings because eventually when added to information gained in the future, they may help to explain the exact mechanism concerned in this phenomenon.

THE ORIGIN OF BILIARY DISEASE

McGowan, Butsch and Walters^{2, 4} had previously demonstrated a spasm of the muscle mechanism at the lower end of the common bile duct following subcutaneous injection of morphine or during attacks of biliary colic. The pain was clearly shown to be due to increased pressure within the common bile duct resulting from the obstructing effect of the spasm. Amyl nitrite and glyceryl trinitrate were found to relax the spasm of the muscle surrounding the lower end of the common bile duct and to result in a lowering of intrabiliary pressure to zero. A series of cases were reported in which repeated attacks of biliary colic were relieved by administration of glyceryl trinitrate gr. 1/100 under the tongue.⁵ Recent evidence has been produced to show that biliary obstruction is produced by duodenal spasm.⁷

We have recently had in our practice the case of a young woman who complained of repeated attacks of biliary colic of recent origin which were relieved by taking glyceryl trinitrate. Roentgenological study showed a normal functioning gall bladder. Fluoroscopic study of the duodenum during an attack of pain showed the presence of a spasm all along the second portion. The study was made while barium was being injected into the duodenum through a small duodenal tube. The movements of the barium within the duodenum presented an interesting picture. The larger part of the

opaque media passed up into the stomach. A small quantity would be forced from time to time into the spastic duodenum. This small bolus would move slowly towards the jejunum until it reached the duodeno-jejunal juncture and then it would pass back in the reverse direction up into the stomach. This suggested to us some motor disturbance in the musculature of the small bowel of which the duodenum is a part. Two days later, during an interval of freedom from pain, similar studies on the same patient showed the duodenum relaxed, the pylorus in an improved state of tone and the peristaltic action of the duodenum normal and in a downward direction. A similar type of peristaltic disturbance had been demonstrated in the duodenum of a patient suffering from the vomiting of pregnancy.¹ Following inhalation of amyl nitrite in the hyperemesis gravidarum case the duodenum appeared to be restored to normal (Fig. 2).

The co-existence of duodenal spasm in patients suffering from the vomiting of pregnancy (Fig. 2) and in those with biliary pain (Fig. 4) suggests to us a plausible theory to explain the etiology of biliary disease. Draper,³ has pointed out that the individuals who are susceptible to gall bladder disease have certain characteristics of the female type. Possibly there is some endocrine excess which leads to a tendency to duodenal spasm which is exaggerated in pregnancy and particularly if there is vomiting. Duodenal spasm at first would produce no symptoms except possibly vomiting. After a period of time the resulting biliary stasis and back pressure would lead to infection and, later, stones.

At first the temporary obstruction in the bile ducts would produce no symptoms because the normally functioning gall bladder regulates the pressure within the biliary system. Later, as the gall bladder becomes diseased its pressure regulating mechanism is lost. Then duodenal spasm would produce back pressure in the biliary system. This pressure at first would lead to a sensation described as fullness in the epigastrium, particularly after foods containing large quantities of fats. Later, as the walls of the gall bladder and the bile ducts become weakened from repeated pressure increases, definite attacks of biliary pain begin to occur. Pain is located in the right upper quadrant and radiates around the right subcostal margin into

the right scapular region. Infection or stones in the gall bladder may act as an aggravating factor in reflexly producing more duodenal spasm. Removal of the gall bladder is followed in a large number of cases by relief of symptoms. In some cases, unfortunately, the pain continues after surgery as before.

PREVENTION AND MANAGEMENT OF POST-CHOLECYSTECTOMY PAIN

When the gall bladder is being removed the common bile duct should be visualized and palpated. If it is enlarged, if stones are felt, or if there had been a history of jaundice the duct should be opened and explored for stones. Other indications for exploration of the common duct are the presence of small stones in a gall bladder with a patent cystic duct, also inflammatory thickening in the head of the pancreas. Zollinger⁹ estimates that exploration of the common bile duct is advisable in 40 per cent of cases with cholelithiasis. Calculi are found in the common duct in 20 per cent of cases which, under these circumstances, are explored. The patency of the papilla of Vater may be tested by passing graduated soft woven catheters down through the common bile duct into the duodenum. A No. 10 F is the size of the average lumen of the papilla in the human being. Zollinger *et al.* have shown that over-dilatation of the papilla of Vater is followed by oedema closing the lumen temporarily. Later, scar formation narrows the lumen of the papilla to less than its previous size.

A T-tube is then placed in the common bile duct. The T-tube drainage decompresses the common bile duct and allows it to return to normal size. This effect alone is beneficial because a normal duct can withstand much more pressure without producing pain than can a dilated one. Further prolonged T-tube drainage seems to allow relaxation of duodenal spasm and a removal of the obstructing factors at the lower end of the common bile duct. These facts were recently demonstrated in two cases on our service.

Two to three weeks after operation, we usually carry out three tests in order to determine the probable duration of the T-tube drainage. (1) The resting intra-biliary pressure is measured. This can be done by connecting an ordinary spinal fluid manometer to the T-tube (Fig. 3). The zero mark of the mano-

meter is placed at the zyphoid level. The resting fluid level in the manometer is ordinarily around this point in normal individuals. (2) The common bile duct is then perfused by running saline in at a pressure of over 300 mm. water above the zyphoid. This procedure normally should not produce pain. In some cases biliary pain similar to that of a previous attack will be produced by pressures as low as 70 mm. water. Such a situation demands prolonged T-tube drainage. (3) Lastly, roentgenograms are taken. Briefly, the method is as follows; 10 c.c. of a warm solution of brominol are injected, by means of a Luer syringe, into the T-tube. An x-ray picture is taken immediately after the injection and again 10 minutes later. In this way the presence of obstruction in the common duct by means of stones, spasm or sphincteritis may be demonstrated. Also it can be determined whether or not the ducts are dilated (Fig. 4).

The patient is then instructed to begin clamping off the T-tube at increasingly long periods starting with one-half hour per day until she can leave the tube clamped off for two weeks and be free from pain. Then the above tests are repeated and the tube removed, only provided; (1) the resting intra-biliary pressure is around zero (*i.e.*, the zyphoid level). (2) Perfusion of the common bile duct with pressures of over 300 mm. water is free from pain and (3) roentgenograms show a return to normal size of the bile ducts with no evidence of obstruction, and with complete emptying after ten minutes. Usually T-tube drainage may be discontinued after three weeks to one month. The T-tube may be left in for six months or more if necessary.

In the post-operative management of patients in which a T-tube had not been put into the common bile duct during cholecystectomy we prescribe glyceryl trinitrate gr. 1/100 with each hypodermic injection of morphine given in order to counteract the spasm producing quality of the latter. During convalescence after a cholecystectomy has been performed patients frequently complain of a sensation of fullness in the epigastrium or of definite attacks of biliary colic. We prescribe glyceryl trinitrate each time any of these symptoms occur and usually prompt relief results. We believe that such procedures discourage biliary stasis

and will do a great deal to prevent the onset of the post-cholecystectomy syndrome.

INTRACTABLE POST-CHOLECYSTECTOMY COLICS

In our practice we have found glyceryl trinitrate successful in the treatment of post-cholecystectomy pain in a large number of cases.⁵ However, in a few instances the results were only partial. One of these concerns a patient who had had her gall bladder removed in 1924. Since 1926 she had suffered almost continuously from biliary pain, vomiting and intermittent diarrhœa. She first consulted us in April, 1937. Frequent doses of glyceryl trinitrate controlled the vomiting successfully but relieved the pain only partially. We operated upon her and found the common duct to be enlarged to over three times the normal. It was opened and explored with scoops. No stones were found. A T-tube was inserted for prolonged biliary drainage. The operative procedure relieved the pain completely. The reason for the failure of the glyceryl trinitrate to relieve the pain can be explained on the basis that the obstruction at the lower end of the common duct which at first was probably functional due to muscle spasm later became organic, due to inflammation and fibrosis (Fig. 5). The relief of pain was due to the lower intra-biliary pressure as a result of the T-tube drainage.

These data tend to indicate that the etiology of biliary disease begins first as a duodenal spasm. There is an increased tendency for duodenal spasm during pregnancy. This may lead to vomiting of pregnancy. This duodenal spasm produces obstruction of the common bile duct which over a period of time produces infection and later stones. This idea was borne out in two cases who recently came under our care. Each patient had been susceptible to attacks of vomiting from childhood; each had vomited excessively with her pregnancies. During the first pregnancy one of these patients began having attacks of biliary colic. This was so severe with the second pregnancy that it became necessary to remove her gall bladder which was filled with stones. The second patient developed her first attack of biliary

colic four months following her second pregnancy, at which time her gall bladder which contained stones, had been removed. Both patients continued to have biliary pain and increasingly severe vomiting even after removal of the gall bladder. Roentgenograms of the duodenum revealed the presence of a spasm in the second portion. We administered glyceryl trinitrate gr. 1/100 three times daily, with the result that their vomiting stopped completely, but the pain only partially subsided. We are now continuing studies in an attempt to find some form of lasting effective therapy for these few intractable cases.

SUMMARY

Studies were made on the duodenum of pregnant women suffering from hyperemesis gravidarum. A marked spasm of the second portion of the duodenum, similar to that known to occur in association with biliary colic following subcutaneous injection of morphine, was found. Amyl nitrite and glyceryl trinitrate (nitroglycerin) have been found to act as relaxers of the second portion of the duodenum. Glyceryl trinitrate has been used successfully for the control of early cases of vomiting of pregnancy and for the relief of attacks of biliary colic occurring after cholecystectomy. The mechanism of its action is the same in both conditions, namely relaxation of the second portion of the duodenum.

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CHANGES IN THE OLFACTORY MUCOSA AND THE OLFACTORY NERVES FOLLOWING INTRANASAL TREATMENT WITH ONE PER CENT ZINC SULPHATE

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EXPERIMENTS were carried out on rats to determine the effect of the zinc sulphate solution used as a prophylactic agent in the poliomyelitis epidemic. A few drops of 1 per cent zinc sulphate in 0.5 per cent sodium chloride solution were introduced into the nasal cavity of a number of animals and at suitable intervals thereafter groups of three or four were killed and the nasal regions sectioned and stained.

The solution was introduced by way of the posterior choanae with the animal held on its back, so that when the nasal cavity was filled the excess solution escaped from the external nares. A sufficient amount of ether anaesthesia was used to permit this procedure. The contact of the zinc sulphate with the mucous membrane was maintained only as long as was required for three to six drops to run through the nose. The animal was then turned head

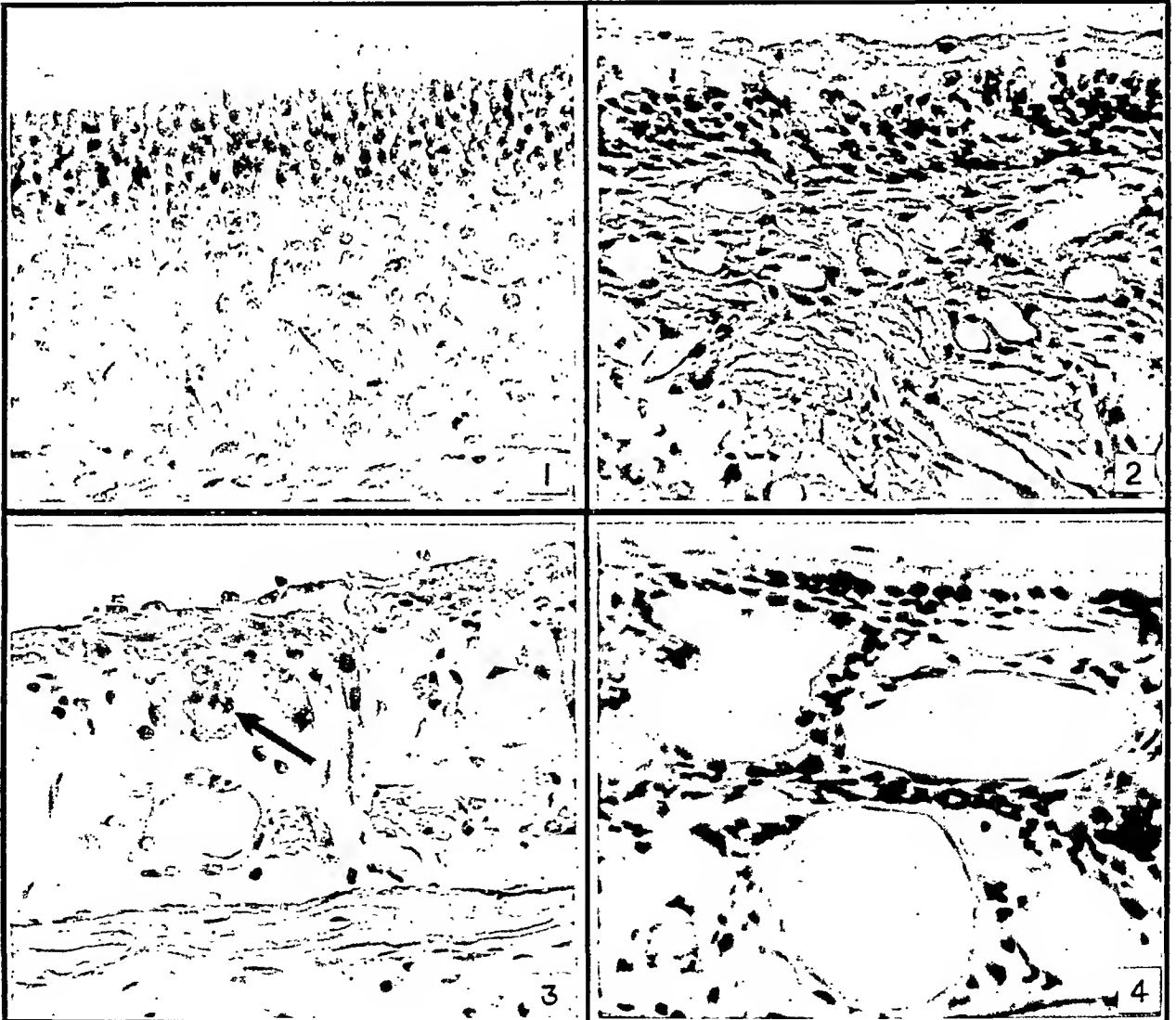


Fig. 1. (x300).—Normal olfactory mucosa. Control. Fig. 2. (x300).—The olfactory mucosa two days after treatment with 1 per cent zinc sulphate. Fig. 3. (x300).—The olfactory mucosa after complete disappearance of the olfactory cells, showing early regeneration. Fig. 4. (x300).—The olfactory mucosa 12 days after treatment showing the differentiation of the regenerated non-sensory elements to form ciliated columnar epithelium.

down and the nasal cavity quickly drained. Observations were made up to two months after treatment. The results presented are based on a study of twenty animals.

Fig. 1 shows the structure of the normal olfactory mucosa. The olfactory sensory cells, actually the perikarya of the olfactory nerve

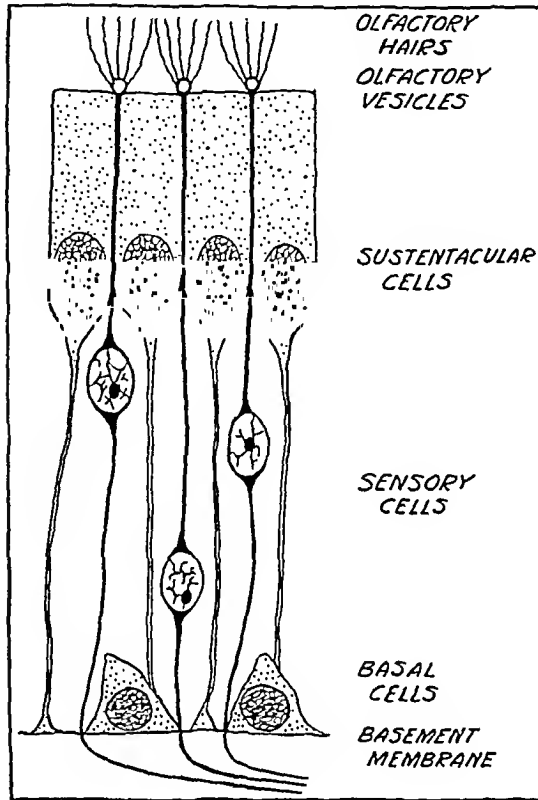


Fig. 5.—A diagram illustrating the structure of the normal olfactory epithelium. The evidence is that all the cells of the epithelium may be destroyed but only the non-sensory cells regenerate.

fibres, are seen in the epithelium crowded six to eight cells deep between the superficial single layer of oval, evenly staining nuclei, belonging to the supporting cells, and the row of basal cells next to the indistinct basement membrane (Fig. 5). The axonal processes of these sensory cells are grouped to form the olfactory nerves which are seen in the tunica propria along with Bowman's glands. The dendritic processes of the olfactory cells pass superficially between the supporting cell bodies to reach the surface, where they expand to form vesicles from which arise the sensory olfactory hairs visible in Fig. 1.

Fig. 2 is a photograph of the olfactory mucous membrane two days after treatment with zinc sulphate. The structural differentia-

tion of the surface has been lost and the nuclei of the epithelium are in varying stages of degeneration. The destruction thus initiated may go on to sloughing, or the necrotic olfactory cells may become enmeshed in regenerating cells derived from the non-sensory elements of the epithelium and then undergo gradual removal. This removal is completed in from seven to ten days after treatment. As early as the seventh day the regenerating cells begin to become cuboidal and develop cilia. Well developed ciliated columnar epithelium is present by the twelfth day. Where locally the tunica propria and the epithelium showed an infiltration with leucocytes this differentiation of the epithelium did not occur.

Fig. 3 shows the regenerated layer of flattened cells covering the surface after complete degeneration of the olfactory epithelium. It would appear that the cells of the ducts of Bowman's glands may act as a source of these new cells, since mitotic figures commonly were found here. A mitotic figure is included in this field (marked by an arrow).

Fig. 4 is a photograph of an area, comparable to that of Fig. 1, from a specimen twelve days after treatment. The thick olfactory epithelium has been replaced by a layer of non-sensory ciliated columnar cells. The tunica propria is much looser, due to the absence of the olfactory nerve fibres which degenerate *pari passu* with the related cell bodies in the epithelium. Specimens studied at intervals up to two months failed to show replacement of these destroyed olfactory cells.

The above description applies to those areas where complete degeneration of the olfactory epithelium occurred. In certain regions not all the sensory cells were destroyed, so that at the twelfth day normal nuclei of olfactory cells with their characteristic nucleoli were sparingly scattered among the supporting cells. Again, in other areas the olfactory cells showed a loss of polarity in that their long axes now lay parallel to the surface. In such a field, since olfactory hairs could not be recognized, the dendritic processes may have been destroyed without killing the cells. If this be the case a loss of function could be expected which would only return when contact with the surface was reestablished. Since patches of these cells could be recognized even up to the end of the second month a study of material three

to six months after treatment will have to be made before the fate of these cells can be determined. Should they again become functional this would offer an explanation for the return of the sense of smell after one to two months in human cases.

In summary, the evidence is, that the three types of cells in the sensory epithelium, (i.e., the olfactory, sustentacular and basal cells, Fig. 5), may be destroyed by 1 per cent zinc sulphate and that replacement of only the non-sensory cells occurs. Work is being done to

obtain further data on the question of regeneration. The results available are presented at this time in order that those who contemplate the employing of this solution as a protective agent may be aware of the destructive (caustic) effect of this salt on the delicate olfactory mucous membrane of the rat, and presumably of man, since histologically the human sensory epithelium is indistinguishable from that of the rat.

The advice and criticism of Professor J. C. B. Grant is gratefully acknowledged.

LARGE SOLITARY CYSTS OF THE KIDNEY

(REPORT OF A CASE)

By S. A. WALLACE

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LARGE solitary cysts of the kidney are comparatively rare. Brown, Deleher and Harpster¹ in 1924 collected only 95 cases in the literature. Eisendrath's textbook of urology (1928) reports 120 cases, and in 1932 McKay² collected 258 cases. The majority of cases apparently occur about middle life, and are slightly more frequent in females. As opposed to polycystic kidneys, which are fairly common and are claimed by some authorities to be definitely hereditary, solitary cysts are very seldom seen in young children, either clinically or at autopsy, and are never bilateral. Large bilateral polycystic kidneys have been seen in children immediately after birth and are quickly fatal.

The etiology of these solitary cysts is not definite, but, as stated by Young, may be due to inflammatory changes resulting in obstruction of the tubules, or to a congenital error of development. Since, however, the condition is practically unknown in children one would be led to believe that it is more apt to be acquired than congenital.

Solitary cysts may attain a huge size. The one reported in this article weighed 7½ lbs. The cysts more often grow from the lower pole, next in frequency from the upper pole, and, lastly, from the convex border. They never communicate with the pelvis but grow from the surface of the kidney. Their walls are thin and fibrous, and no doubt composed originally of thinned-out parenchyma as they are so closely adherent to the kidney that it is impossible to

shell them off. The contents are usually serous but occasionally hæmorrhagic. Traces of albumin, salts and urea may be found.

The diagnosis is sometimes rather difficult. The symptoms complained of are caused by pressure of the cyst, and usually are abdominal distension, breathlessness, and a dull ache in the side. Sometimes pressure symptoms on the large bowel may occur. If the cyst is of moderate size it may be felt attached to the kidney, usually the lower lobe. On the other hand, it may be so large as to fill practically the whole abdomen, and it may be almost impossible to tell its nature before operation. The urine is quite clear and symptoms such as frequency or dysuria are not present. The pyelogram may show no distortion whatever unless the cyst is growing from the lower pole and producing pressure on the ureter or lower calyx. This would probably suggest tumour rather than cyst. The urine obtained from the affected kidney may be quite normal and the thalein test satisfactory. The pyelogram, however, may show the pelvis of the kidney pushed well away from its normal position. It may be seen down towards the pelvis or pushed toward the mid-line, or, as in the following case, the pelvis of the right kidney may be displaced across the mid-line and seen to be superimposed over the pelvis of the left kidney. The plain x-ray may show the tumour outline and an absence of bowel over it, or a barium enema may show the large bowel curving around the tumour or thinned out

barium passing over it. Aspiration of a cyst may be done through the loin, as performed in the present case, if one is sure it is retroperitoneal, and examination of the fluid obtained may give some clue as to its origin. In the differential diagnosis one has to exclude ovarian cysts, dermoid cysts, retroperitoneal cysts, hydatid disease, and cysts of liver, pancreas, spleen or mesentery.

margin. The mass was dull on percussion and this dullness continued around into the flank.

Pelvic examination was negative. Plain x-ray showed no gas or bowel loops in the right side of the abdomen. Gall-bladder dye did not give a shadow in the x-ray. Cystoscopic examination showed a normal bladder, and both ureters were easily catheterized. Specimens from each side proved to be normal. The iodide solution seemed to run out of the right catheter very quickly. Seven c.c. were injected into each pelvis. The pyelogram was rather difficult to read, and indicated, we thought, either a double kidney or the pelvis of the right kidney pushed over till it was



Fig. 1



Fig. 2

Fig. 1.—Double pyelogram showing the right pelvis overlapping and lying beyond the left pelvis. Fig. 2.—Showing specimen immediately after removal.

The treatment must be surgical if the cyst is large enough to produce pressure symptoms. Fortunately, in solitary cysts no nephritic signs are present, such as accompany polycystic kidneys. If an attempt is made to save the kidney the sac must all be removed before stitching the kidney over. In cysts of the lower pole a partial nephrectomy might be done. In the case of large cysts the usual treatment is total nephrectomy.

CASE REPORT

Mrs. D., aged 52, was referred by Dr. Beech, of Salmon Arm, on July 11, 1937. Her symptoms were discomfort from abdominal pressure and shortness of breath. For a period of about ten years she had noticed a swelling in the right side of the abdomen which had gradually increased. There was no history of colic and no urinary signs had been noted. Since the patient was rather short and stout it was hard to palpate the tumour definitely, but it seemed to fill the right side of the abdomen and come from the right kidney area. It was rather difficult to get the fingers between the tumour and the right costal

superimposed over the left, and really beyond it, as seen in the accompanying illustration. Aspiration in the right loin under local anaesthesia was done and clear fluid obtained.

At operation, July 16, 1937, a long vertical incision lateral to the right rectus was made. On opening the peritoneum a large subperitoneal cyst was seen, with the caecum and ascending colon riding over the top of it. A fairly long incision over the posterior parietal peritoneum was made just lateral to the caecum and ascending colon, and the cyst isolated by finger dissection. The right kidney which was flattened out over the cyst was found beyond the vertebral column and even lateral to the left kidney. The right ureter was isolated and divided, the stump cauterized, the pedicle clamped and divided, and the cyst removed intact. A small drainage tube was placed behind the peritoneum.

Convalescence was smooth and the patient left the hospital in two weeks, feeling quite well.

The pathological report of Dr. A. G. Naismith follows: "Kidney with large solitary cyst arising from the outer aspect of the right kidney. There appears to be no direct connection between the cyst and the pelvis of the kidney, and, though thinned out, there is kidney tissue continuous between both the upper and lower poles. These poles appear slightly larger and a deeper red in colour than usual. The cyst

weighs $7\frac{1}{2}$ pounds, is ovoid in shape, and measures 25 cm. x 16 cm. x 9 cm. The wall of the cyst is composed of firm, fibrous connective tissue about 1 mm. thick, and showing blood vessels on the surface. The contents were quite clear; specific gravity 1.005, and contained no cells or albumin. Close examination of that part of the cyst in direct apposition to the

kidney showed no apertures connecting it with the kidney."

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RECURRENT INTRA-OCULAR HÆMORRHAGE IN YOUNG ADULTS (EAL'S DISEASE) (REPORT OF A CASE*)

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IN 1880 Henry Eales,¹ of Birmingham, published a report on "Cases of retinal hæmorrhage associated with epistaxis and constipation". In this first paper he described five cases of recurrent retinal and vitreous hæmorrhage, all in young men, their ages ranging from 14 to 29 years. He described symptoms of high arterial tension, such as slow pulse and accentuation of the heart sounds, but found no further evidence of constitutional disease of any sort. He attributed the condition to a neurosis affecting the circulatory and digestive systems. In all the cases the left eye was mainly affected, though in one the right eye was also involved. This, he thought, was because the left carotid artery arises more directly from the aortic arch than the right and the course of the left innominate vein is longer and more indirect than the right. These circumstances, he believed, produced slightly greater capillary tension on the left. According to Krause,² von Graefe in 1855 had described periodical intraocular hæmorrhage in young persons who had often had previous epistaxis. He wrote:

"I have treated patients who have, merely periodically, suffered from intraocular hæmorrhage, destroying sight completely, at intervals of several months. It is peculiar that the patients were nearly all young individuals in the twentieth, thirtieth and rarely fortieth years of age. In a few cases a complication of apoplectic attacks indicated vascular disease. In many, there had been previous nasal hæmorrhages which had ceased since the ocular hæmorrhage. In two cases, there seemed to be a relationship with hæmorrhoidal bleeding and in another the cessation of perspiration of the feet."

Jonathan Hutchinson³ in 1880, a few months after Eales' article, described a case of primary intraocular hæmorrhage in the left eye, which was later removed because of glaucoma. Two years later the right eye was similarly affected

with hæmorrhage. The patient suffered from epistaxis and constipation, and here also, while there was no sign of constitutional disease, there was a strong family history of gout. Hutchinson attached importance to inheritance of the gouty state, and disagreed with Eales on the importance of constipation as a starting point.

In 1882 Eales⁴ published a second paper on "Primary retinal hæmorrhage in young men". He suggested the name "primary recurrent retinal hæmorrhage" and again outlined the characteristics of the disease. In each case it was the left eye which was primarily and chiefly affected. All were young men, the youngest being 14, the oldest 20. All had been subject to epistaxis, especially during the summer months, and all had suffered from constipation. All were much troubled with dyspepsia, low spirits, want of energy, and a feeling of lassitude. It is remarkable, writes Eales, that in no case has a similar condition been seen in a female. He thinks possibly the menstrual function acts as a safeguard against this serious malady. The retinal hæmorrhages were described in detail. They were large and round or irregular, and as a rule confined to the periphery of the retina. The vision suffered in proportion to the vitreous opacities, which often cleared very rapidly between the attacks. The end-results were large whitish glistening patches in the periphery of the retina and branched vitreous opacities. Sometimes small retinal detachments occurred.

Nieden⁵ in 1882 reported that in 34,489 consecutive eye cases in eight years and six months he had found only 6 patients suffering from idiopathic recurrent vitreous hæmorrhages. In three cases, the second eye was not involved; in the other three, both eyes were affected alternately. Of the nine eyes affected in his six cases, five were the right and four the left.

* Case shown at the Medico-Chirurgical Society meeting, Montreal General Hospital, December 3, 1937.

There was no history of gout, syphilis, diabetes, tuberculosis or constipation, although there was loss of appetite and lassitude. In discussing Nieden's paper Schweigger⁶ remarked that he had observed similar cases among young women. Henry⁷ in 1894 described a typical case in a young man of 19 years, in which the right eye was affected, the left remaining normal. He suffered from headache, constipation and epistaxis. The retinal hæmorrhages were chiefly peripheral. Krauss,² in 1908, reported a case in a young man of 23 years, who suffered from constipation but not from epistaxis. The right eye alone was affected. Recurrent vitreous hæmorrhages were frequently preceded by severe headaches. Rapid recovery of vision took place between the attacks. Areas of "choroiditis" and vitreous veils were left by the disease.

Davis⁸ in 1912 reported a case in a young man aged 22 years who was the subject of dyspepsia. However there was no history of constipation. He had hæmorrhages in the retina and vitreous of each eye. Within a year he had lost the vision of the right eye, in which the hæmorrhages had begun. The left one had also become seriously impaired. In this case there were intervals when albumin was present with many casts in the urine. Vitreous opacities, retinitis proliferans, and retinal detachment resulted from the disease. Davis believed that the hæmorrhages arose from the retinal and not from the choroidal vessels. He concluded that tuberculosis, indigestion, and autointoxication were definite etiological factors, and suggested tuberculin and general hygienic management in its treatment. Bennett⁹ in 1913 reported a case of a woman aged 23 years with retinitis proliferans in the left, and incipient retinitis proliferans and small retinal hæmorrhages in the right eye. There was no history of epistaxis or of constipation.

In 1920 Zentmeyer¹⁰ reported four cases that he had seen. The Wassermann reaction was negative in all four; in two, the von Pirquet test was positive. Coagulation of the blood was delayed in two cases. Zentmeyer did not entirely reject tuberculosis as a cause, but thought some other factor must be found. In view of the constant age incidence, the frequency with which males were affected, and the benefit derived from the use of thyroid extract, suggested to him that a disturbance in the activity of the ductless glands might be a factor. Possibly deficient activity in the adrenals caused lack of tone in

the venules and predisposed to hæmorrhage. Aubineau¹¹ in 1920 reported five cases of intra-ocular hæmorrhage in adolescents, and Finnoff¹² in 1922 reported five cases in males; three of these were over 30 years of age—one aged 42 years was the subject of pulmonary tuberculosis. Finnoff concluded that this was not a specific disease, and that tuberculosis of the retinal vessels, especially the veins, was a common etiological factor. Young¹³ in 1930 reported three cases of recurrent hæmorrhage into the retina and vitreous in adolescents. One case showed deficiency in blood calcium, and seemed to benefit from the administration of calcium.

In 1932, H. P. Hutchinson¹⁴ reported five cases, four males, one female, between the ages of 17 and 25 years. Two patients were definitely lacking in spirits and energy. In two there was a history of epistaxis, in one other case epistaxis occurred during the course of the disease, although it had never happened before. In no case was constipation present. Discomfort and flatulence after food were complained of in two cases. Frontal headache was a feature in two cases. In no case was any sign of tuberculosis found. There was no suspicion of syphilis, congenital or acquired, in any case. The blood Wassermann and Sigma reactions were negative in each case. Blood counts done in four cases were normal.

In all five cases both eyes were involved to a greater or less extent. Vitreous hæmorrhage occurred in all cases. In one, the vitreous hæmorrhage was slight and the vision after recovery was good. In the other four cases the vitreous hæmorrhages were large, and the vision after recovery very poor. The retinal hæmorrhages in three of the cases were mainly peripheral. In three cases in which large vitreous hæmorrhages occurred permanent vitreous opacity had resulted. Vision was reduced in the affected eye to 6/60 in one case and to even less in the other two patients. In the case in which the vitreous hæmorrhage was slight the vision is now 6/6 in both eyes, three years after the last hæmorrhage. A few veil-like opacities with delicate new vessels project from the retina into the vitreous of the affected eye in this case. Complications such as detached retina, chronic glaucoma, and iritis had not occurred up to time of the report.

CASE REPORT

F.S., an adult male of 24 years, presented himself at the clinic in October, 1932, complaining that his left eye had become suddenly blurred the previous day. He was a spare youth, fairly well nourished and apparently in good health, but seemed lacking in spirits and energy. Examination showed three large retinal hæmorrhages with blood in the vitreous. He was advised to enter hospital for a complete physical examination.

His general physical condition was found to be practically normal. Blood pressure, 142 over 90, urine normal, blood normal, bleeding time and blood coagulation normal, blood platelets and blood calcium normal. Wassermann negative. Questioned directly about constipation he stated that he had never been troubled in this respect. He complained though of general lassitude and seemed in low spirits. An interesting fact was elicited in that he gave a definite history of frequent attacks of epistaxis up to about his 16th year. Since that time he had been free.

The left fundus showed above the disc and to the temporal side a large retinal hæmorrhage, while below and to the temporal side, along the inferior temporal artery there was seen a large preretinal hæmorrhage. There were also a number of small retinal hæmorrhages. There was blood in the vitreous. The right fundus showed no hæmorrhages and his right vision was normal. In due course he was discharged from the ward and kept under observation in the out-patient department.

In the following November he complained of fresh spots before the eyes from the previous day. Examination showed in the left eye fresh hæmorrhages fimbriated above and below from the capillaries (retinitis proliferans—vitreous opacities). He was seen again in February, 1934, stating that he had had further disturbance in the left eye, and examination showed a fresh hæmorrhage along the vein in the lower inferior nasal quadrant. In March and June, 1934, he again reported fresh hæmorrhages in the left eye. He had now become quite apt, not only in noticing the hæmorrhages, but also the speed of absorption, etc., and would report on the degree of hæmorrhage and the speed of repair. At this period he was advised to proceed to a mountain resort. Local treatment and medication had not had the slightest effect, and it was thought that the routine life of a sanitarium would benefit his general health and thus improve his eye condition.

In December, 1935, he again appeared, having been in the mountains for some months, and complained of a large hæmorrhage in the left eye. This hæmorrhage was so severe that it was impossible to illuminate the interior of the eye at all. The right eye still appeared normal, with vision 6/6. On April 17, 1936, and August 14, 1936, hæmorrhages in the left eye were again noted. On October 19, 1937, he was once more examined, and a number of fresh hæmorrhages in the left fundus seen, as well as a number of old ones. His right vision was normal. He appeared next on February 21, 1938, and reported he had had a severe hæmorrhage in the left eye on February 16th, "this however was clearing quickly". His left vision was 6/36. There were numerous opacities in the vitreous, so that little detail of the retina could be made out. His physical appearance, as well as his spirits, were now much improved.

This case in its general characters is identical with those described originally by Eales. A young man of 24 years, who has suffered from retinal hæmorrhages in the left eye for a period of six years. Between attacks the vision improved to marked limits. The left vision is noted at different periods as 6/12, 6/36, 6/9. In October, 1937, his vision had recovered to 6/6. At present writing it is 6/36.

The chief interest in these cases is the question of etiology, which is still unknown. Eales' theory that constipation played an important rôle in this respect, has not received much sup-

port; also blood changes such as delayed blood coagulation, prolonged bleeding time, and deficiency in blood calcium have been ruled out. The theory that tuberculosis is an etiological factor lacks sufficient evidence. Zentmeyer suggested a disturbance in ductless gland activity, that adrenal deficiency might cause lack of tone in the venules and predispose to hæmorrhage. Hutchinson¹⁴ suggests "it is most likely that there is some abnormality of the blood, as yet unrecognized by pathological tests; it might be a deficiency of some normal constituent, producing reduced viscosity or altered osmotic pressure, or it might be the pressure of some abnormal toxic constituent, absorbed from the bowel. The general condition of lassitude and low spirits, so common in the subjects of the disease, supports this view."

Eales' is a rare disease and before a diagnosis is made it is necessary to exclude other conditions in which such hæmorrhages may occur, such as nephritis, diabetes, the anæmias, purpuras and syphilis. The prognosis, as the disease is confined to the eye, refers to vision and is bad. Recurrences are likely for months or years with greater or less injury to vision. The ultimate prognosis depends on the magnitude of the hæmorrhages and their damage to the retina and vitreous. No consistently successful method of treatment has been reported. Treatment in the way of general hygienic measures should be adopted. Potassium iodide, calcium and parathyroid extract have been recommended. Tuberculin has been used therapeutically and with some reported success. Local treatment insuring rest of the eyes as long as the hæmorrhages continue is important. No consistent success, of any form of treatment, has as yet been reported.

CONCLUSION

A case of Eales' disease, occurring in a young man of 24 years, who gave a history of epistaxis through childhood is reported. There was no history of constipation or dyspepsia, but lassitude and lowered vitality were prominent. The hæmorrhages have been observed over a period of six years. They have always occurred in the left eye. The retinal hæmorrhages have not been specially peripheral, and have usually been accompanied by hæmorrhages into the vitreous. After this lengthy period, the vision though defective is still one-sixth of normal. The etiology is unknown and treatment has likewise been unsatisfactory.

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A TRIAL STUDY OF 1,800 CASES OF SYPHILIS INFECTED TWENTY YEARS AGO

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ONE of the greatest difficulties confronting any research into the sequelæ of syphilis is the lapse of time between the date of infection and the appearance of certain types of sequelæ. It is almost impossible to find a portion of any population so static that cases may be followed from infection to total disability or death. Studies on syphilis may therefore be divided into two parts: (1) the primary infection and its treatment; (2) the diagnosis and treatment of sequelæ. Between the two there usually exists a gap or silent period. This period may be anything from 1 to 35 or more years, but with an average of 10 to 15 years. It is therefore usually long enough to disrupt the sequence of any study largely because of shifting populations. In ordinary clinic practice fresh infections are treated until the disappearance of symptoms, and then in most instances the patient is lost sight of. It is not possible to follow all cases treated through a long period of years and therefore the percentage developing after-effects is not correctly known.

In the second instance, when sequelæ are discovered, it is quite impossible to know the total number of infections out of which they arose. Estimates have been made, but show wide variations. Hinton, in his book on "Syphilis and its Treatment", page 117, states:

"The percentage of syphilitics who become significantly affected with neurosyphilis is hard to estimate from most statistics, for generally they give the per cent of neurologic cases due to syphilis, but do not give the per cent of syphilitics who manifest symptoms of tertiary neurosyphilis."

The chief purpose of this study is to evaluate the efficacy of the treatment given during the war years, and to discover, if possible, the number of sequelæ that have occurred in the intervening 20 years. The prevention of sequelæ is considered of infinitely more importance from the standpoint of permanent

disability and untimely death than the disappearance of early symptoms, realizing of course that these latter must be taken care of for public health reasons.

Following the early policy of the Director-General of Medical Services, to combat the spread of the venereal diseases in the army and to adequately treat those infected, it was necessary to establish a tolerance level for the arsenical compounds used in treating syphilis because of certain evidences of toxicity, and in order to obtain the maximum therapeutic effect. The records indicate that six to seven injections of an arsenical compound, and a similar number, or more, of mercury were considered adequate to cure or arrest most cases, and this amount of treatment will be referred to hereafter as a course.

We think it must be agreed, in the light of our knowledge of arsenicals in the war years, and since the supply of original 606 from Germany had been cut off, and new but similar preparations were being used that were still untried by time, that probably courses, as indicated above, were properly considered as intensive treatment at that time, while at present they would be considered inadequate. However, as results are of more importance than any standard of dosage, the number of sequelæ that have developed in the intervening 20 years may be considered as the measure of efficacy for the treatment carried out by the Canadian Army Medical Corps during the war.

The information for this study is being taken from several sources: (1) the admission and discharge books of the special hospitals; (2) the original overseas documents which contain the special treatment form with symptoms, amount and type of treatment, and usually the final Wassermann reaction; (3) the files that have been created since discharge from the

expeditionary force and which contain a record of any contact with the department for any reason, between demobilization and the present time; (4) other departmental records such as hospitalization, treatment, and death cards.

ANALYSIS OF 1,800 CASES
1,518 are estimated to be alive
282 are known to be dead
ORIGINAL DIAGNOSIS

Primary:	Total	Known dead	Estimated living	Percentage of total
1. Chancre of genitalia....	1,523	237	1,286	87
2. Chancre of other sites..	38	3	35	
Secondary:				
3. Chancre, rash, positive Wassermann and secondary symptoms ...	214	34	180	12
Tertiary:				
4. Without central nervous involvement	8	1	7	1
5. With central nervous involvement	13	7	6	
Congenital:				
6. Congenital	4	0	4	
Totals	1,800	282	1,518	100

It will be seen from the above that 87 per cent were fresh infections and only 12 per cent had developed secondary symptoms, while 1 per cent were tertiary of pre-war date. The exact date of infection is stated in 87 per cent of the cases and the exact or approximate date in another 12 per cent. Of the 282 dead only a few (19) died from the direct results of syphilis. This will be dealt with under sequelæ.

HOSPITALIZATION

Those estimated to be alive averaged 2.2 months in hospital; those known to be dead averaged 3.2 months in hospital; the total average of hospitalization is 2.3 months.

TREATMENT

A course consisted of approximately 7 injections of some arsenical compound, and 7 or more injections of mercury; 1792 of the 1800 men received the combined treatment, 3 were given Hg. and iodides, and 4 had hyperpyrexia at some later date. Except in certain instances, where sequelæ developed, the records do not indicate that these men availed themselves of treatment following demobilization, although it is realized that some may have done so.

It is also probable that a few developed sequelæ of which we have no knowledge, but our chief neuropsychiatrist believes the number to be very small.

NUMBER OF COURSES GIVEN

		Percentage
One course	1,226	68
Two courses	350	19
Three courses	120	8

A few others had from 4 to 6 courses, while 33 had prolonged treatment with various drugs. There is only one case where the amount and type of treatment are unknown.

WASSERMANN REACTION

In the majority of cases a man was discharged from hospital (overseas) when his Wassermann test was negative.

		Percentage
Negative Wassermann	1,290	72
Positive Wassermann	267	15
Unstated Wassermann	243	13
Totals	1,800	100

From the amount of treatment given, as indicated by the records, it is quite likely that a fair number of the unstated were also negative, although the treatment sheet bears no entry of a final Wassermann test.

SOCIAL HISTORY

Under this heading, we made an attempt to find out what had happened to these men in the intervening years and if it is kept in mind that 75 per cent of the cases have post-war files in the department it may be assumed that if a physical, mental, or economic breakdown had taken place, there would, in all likelihood, be a record in the man's docket.

	Total	Known dead	Estimated living	Percentage estimated living
Died on service	103	103		
Estimated normal	1,028	100	928	61.0
Broken employment	101	17	84	5.5
War veterans' allowance..	57	9	48	3.0
Bad social history	19	2	17	1.1
Unemployed, physical disability	59	23	36	2.3
Unemployed, mental disability	9	2	7	0.5
Penitentiary	4	1	3	0.02
Mental deterioration, institutional	29	15	14	0.9
Unstated, documents only.	391	10	381	25.0
	1,800	282	1,518	100.0

As far as we can judge, over 60 per cent appear to be self-supporting and able to work. Only 5.5 per cent are recorded as having a broken employment record; 3 per cent are on

War Veterans' Allowance or "Burned Out". The most surprising factor is the small number mentally incapacitated, for we find among those estimated alive in this group only 0.5 per cent are not institutionalized and 0.9 per cent are in institutions. Further, not all of the mental disability is stated as due to syphilis. Twenty-five per cent have no record, and in all probability most of them are self-supporting, since they have not contacted the department for any reason, either economic or because of mental or physical disability.

When taking out information, we noted, where possible, any other morbid condition, accident or violent death, and a study of these conditions leads us to believe that in this group, who are primarily syphilitic, there follows the usual morbid conditions found in any cross-section of the population, keeping in mind age and sex.

SEQUELÆ

	Total	Known dead	Estimated living
Number estimated free of sequelæ	1,686	254	1,432
Number with sequelæ	114	28	86
Total	1,800	282	1,518
Total cases	1,800		
Total sequelæ	114 or 6.3% of total cases		
Total estimated living ...	1,518		
Sequelæ diagnosed	86 or 5.6% of living		
Total dead	282		
Sequelæ diagnosed	28 or 9.9% of dead		

Apart from tabes and G.P.I. sequelæ in many cases do not appear to hasten death; even those with involved hearts live many years.

DISTRIBUTION OF SEQUELÆ

	Total	Known dead	Estimated living
1. Cardiovascular system	7	4	3
2. Gastro-intestinal system	2	1	1
3. Respiratory system	4	0	4
4. Bones, joints and muscles...	4	0	4
5. Genito-urinary	1	0	1
6. Eye (with no other involvement)	23	3	20
7. Nervous system	60	18	42
8. Cerebral symptoms	4	1	3
9. Spinal symptoms	2	0	2
10. Sequelæ cured or arrested ..	7	1	6
Totals	114	28	86

DETAILS OF SEQUELÆ

All infections, except a few pre-war, occurred during the war.

1. *Cardiovascular system*.—Hypertrophy and dilatation, myocarditis, endocarditis, coronary arteries, pericarditis, aortitis, gumma, phlebitis,

vascular lesions, cardiac neuroses: 7 cases, 4 dead, 3 alive. The average lapse of time between infection and the diagnosis of sequelæ is approximately 10½ years, the actual time varying from 1 to 19 years. In some cases the relationship of syphilis to the cardiovascular condition seems very slender, and we must also bear in mind the examiner knew the specific infection existed. The 4 who died are recorded as dying of cardiovascular disease. Cardiovascular sequelæ constitute 6 per cent of the total. The average age at discovery of sequelæ was 40 years.

2. *Gastro-intestinal*.—Gumma or ulcer of the œsophagus or stomach, gumma or ulcer of the intestines, liver frequently affected from jaundice, gummata, acute yellow atrophy: 2 cases, 1 dead, 1 alive. The one death was due to gastro-intestinal condition. The average lapse of time between infection and diagnosis of sequelæ was 11 years, the actual time varying between 4 years and 18 years.

3. *Respiratory system*.—Catarrhal laryngitis, tracheitis, bronchitis, syphilitic phthisis: 4 cases, all alive. Average lapse of time between infection and diagnosis of sequelæ was 10 years, the actual time varying between 4 to 15 years.

4. *Bones, joints and muscles*.—Gummata, osteitis, arthralgia, synovitis, arthritis, myalgia, myositis: 4 cases, all alive. Average lapse of time between infection and diagnosis of sequelæ was 15 years, the actual time varying between 1 to 25 years.

5. *Genito-urinary system*.—Gumma of bladder, hæmaturia: 1 case, alive. Lapse of time between infection and diagnosis of sequelæ is 6 years.

6. *Eye*.—Iritis, optic neuritis, optic atrophy, choroiditis, paralyzes of ocular muscles: 22 cases plus 1 congenital—23 cases; 20 alive; 3 dead (not due to syphilis). Average lapse of time between infection and diagnosis of sequelæ was 3 years. Out of the 23 cases, 3 were delayed in exhibiting sequelæ, taking 9, 10 and 19 years. The balance were all within 5 years, and of these, 15 were within a year.

Sequelæ involving the eye differ from all other sequelæ in manifesting themselves much earlier and constitute about 19 per cent of the total number. Average age at discovery of sequelæ was 28 years.

7. *Nervous system*.—Paresis, tabes, etc.: 60 cases, 18 dead, 13 died of sequelæ, and 5 of other causes not related to syphilis. Average lapse of time between infection and diagnosis of sequelæ was 10 years, actual time varying from 1 to 33 years. There appear to be three stages in the lapse of time in the sequelæ of the nervous system: (1) sequelæ appearing within a year or very close to the infection; (2) those appearing from 10 to 15 years after infection; (3) a few appearing after a prolonged silent period up to 33 years. (These latter are pre-war infections, with the date supplied by patient but probably correct). The sequelæ under this head constitute 52 per cent of the total 114 conditions attributed to syphilis, but only 3.3 per cent of the 1800 cases studied. Average age at discovery of sequelæ was 35 years.

8. *Cerebral symptoms*.—Meningitis, gummata, cranial nerve involvement, optic neuritis, etc.: 4 cases, 1 dead of sequela. Average lapse of time between infection and diagnosis of sequelæ was 8 years. Two of these cases developed within 1 year, the others at 14 and 17 years. Average age at discovery of sequelæ was 34 years.

9. *Spinal symptoms*.—Ataxic paraplegia: 2 cases, alive. One developed symptoms in 1 year, and in the other the date of infection is unknown.

10. *Sequelæ cured or arrested*.—These may be in any group from 1 to 9; 7 cases, 1 dead of other causes. Average lapse of time between infection and diagnosis of sequelæ was 3 years, 4 of the cases being diagnosed approximately within a year, and the balance about 9 years afterwards.

SOME FIRST IMPRESSIONS

The amount of treatment received by these men overseas, when the infection was fresh, seems to have reduced the expected crop of sequelæ to 6.3 per cent of the total infections, and, as this figure includes a number of pre-war infections among older men whose sequelæ were discovered and treated during the war, and many of whom have since died, the figures should probably be lower, since we find only 5.6 per cent of those now living suffering from sequelæ, the result of infections contracted 20 years ago. Apart from the 3.3 per cent of those who contracted tabes, G.P.I. or a cerebro-

spinal condition, the amount of severe disability existing is surprisingly small. Among the 114 cases are some that have a borderline diagnosis, but which are included to be on the safe side.

Prior to the introduction of the malarial and tryparsamide treatment, certain cases of tabes and general paresis quickly went on to great physical or mental deterioration in spite of the utmost that treatment could accomplish, and our findings suggest that the number so affected is probably 3 to 4 per cent of the total men infected, indicating that, as in many other conditions, there are a few individuals who are unable to develop a defense mechanism even with the aid of extensive drug treatment, although malarial and tryparsamide treatments are retarding deterioration in a percentage of these cases. This is in contrast to the remaining 95 per cent of those infected, who, with very little treatment, such as the one course administered overseas, have been able to escape sequelæ altogether, or have had their latent manifestations delayed beyond 20 years. This may raise the question of the value of prolonged and intensive treatment where the only sign of involvement is a weakly positive Wassermann reaction.

Eye conditions, with no other involvement, are the second largest group, and differ from the others in that the bulk of them appear within a year of infection and attack the younger individuals, the average age at discovery being 28 years. None of the 23 patients in this group have died of syphilis so far as we can ascertain.

The study would appear to indicate that the white male is probably developing a certain amount of resistance to the ravages of syphilis, more so than in most chronic conditions, such as tuberculosis, for in what important chronic disease after a lapse of 10 to 20 years do we find only 6 per cent with permanent damage, and of those only one-sixth dead of the disease? (1,800 infections, 114 sequelæ, 86 alive, 28 dead, of whom 19 died of the disease).

We do not wish at this juncture to attempt any conclusions, as they would be premature, but, from the way the figures are running, it is likely that we shall find a smaller number of sequelæ than anticipated, and that many of them do not incapacitate to the extent formerly thought.

THE SIGNIFICANCE OF EPIGASTRIC HERNIA*

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ALTHOUGH epigastric hernia is a relatively common condition, little has been written on the subject, and in what has been said there seems to be considerable variation in the interpretation of the significance to put on the finding of such a hernia in a patient with abdominal visceral symptoms. In this paper a brief review of the literature to date will be given, and also an analysis of 46 cases of epigastric hernia admitted to the Royal Victoria Hospital during the past ten years. Thus I hope to be able to indicate the importance of, and the procedure in, the different types of epigastric hernia. This paper has been written to fill the need of a uniform method of approaching and treating this condition.

Etiology.—The great majority of such herniæ are acquired and due to strain. This strain may be of the acute variety, the hernia appearing shortly afterwards. About 20 per cent of patients with this condition will date their hernia to some excess muscular effort, this being most marked in the labouring class. Chronic prolonged strain on the abdominal muscles, as in constipation with straining at stool, chronic cough, vomiting, etc., results in many of the remainder. Prolonged illness and emaciation are definite predisposing causes.

The idea of a congenital defect in the wall being a causative factor seems quite unlikely, except in the very rare case. No preformed sac is present as in the inguinal type of hernia; also, the age incidence is about middle life. If such a defect were present the area would have only the barrier of the transversalis fascia to penetrate, and would thus appear at an early age.

Lothrop in 1897 gave the following classification of epigastric herniæ: (1) embryological defect due to failure of fusion of part of the abdominal parietes; (2) weakness of the abdominal muscles following emaciation; (3) a small defect in the fascia usually due to some type of strain or trauma through which the preperitoneal fat pushes its way, and which may

or may not be followed by a pocket of peritoneum. Omentum and intestine may be found in the sac. It is only the last one in this classification that has any practical value, as it accounts for the great majority of cases.

Pathology.—It is of interest to review the structure of the region involved. The linea alba is composed of the fusion of the aponeuroses of the external oblique, internal oblique and transversalis muscles, and is a dense and relatively avascular structure. Beneath this are the transversalis fascia, the preperitoneal fat, and finally the peritoneum. The preperitoneal fat is massed to the right of the midline in the falciform ligament of the liver which carries the obliterated umbilical vein in its free edge. The posterior rectus sheath and transversalis fascia are perforated by numerous vessels running to the preperitoneal fat and peritoneum, derived from the lower intercostal and superior epigastric arteries. These perforation spots are weak areas, and it is reasonable to suppose that increases in intra-abdominal pressure will cause an initiation of the herniation, which is always fatty tissue at the start. The linea alba being strong and having few blood vessels, the perforations usually occur at one side or the other of the midline, and may even come through the rectus at its lateral edges. The original perforation hole is gradually enlarged to an oval ring, and, due to the increase of the fatty protrusion, the peritoneum is gradually pulled upon and a sac is formed. This is well borne out by the fact that the small epigastric herniæ seldom have a well-defined sac, while the large ones almost invariably have. The sac is, of course, covered by considerable fat, as in a femoral or direct inguinal hernia. The entrance of omentum or intestine is thus made possible. The stomach is rarely seen in the sac.

Epigastric herniæ are thus of two anatomical types, the first a preperitoneal mass of fat united to the peritoneum by a pedicle, and the second a true hernial formation with a sac. The first variety is the more common as it is the early stage of the condition, but the majority of those for which surgery is necessary contain a

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sac. In 33 operations on epigastric hernia in the present series, 20 had a sac, and in 13 no sac was found. In 39 cases reported by Denk an empty hernial sac was found in 20, free omentum in 5, adherent omentum in 7, and transverse colon and stomach in 1 case. There were 6 cases of fatty tissue without hernial sac. Omentum was the only viscus found in this series to be present in the sac, being adherent in 6 cases and free in 1 case.

Incidence.—The majority of epigastric herniæ occur in men, particularly of the labouring class. Our average age was 42.4 years, and the males outnumbered the females by 42 to 4, or a percentage of 91.3 to 8.7. Kuttner reports 59 males out of a total of 65 cases.

As is well known, epigastric hernia is frequently associated with other types of rupture, 10 of our cases having other types of hernia present or previously repaired. However, the epigastric variety forms a very small percentage of all types. The figures of the various writers vary from those of Berger, who gives the epigastric type as 0.08 per cent of all herniæ, to that of Imfield, who reported 450 consecutive hernia cases, with 21 of the epigastric type, or 4.6 per cent.

At the Royal Victoria Hospital in the past ten years there have been 2,299 cases of hernia exclusive of the post-operative or recurrent varieties and 46 of the epigastric variety, or 2 per cent.

Diagnosis.—As previously mentioned, the minority of cases appear suddenly, following strain or marked exertion. The chief complaint in these is pain in the epigastrium, which may vary from a constant ache to that of acute colic. Radiation may occur in any direction. The pain is aggravated by exertion, straining, or the upright position, and is relieved by lying down, unless incarceration has occurred. Nausea and vomiting are usually present. The hernia can be felt as a definite mass, usually about half-way between the umbilicus and xiphoid, and varies between the size of a cherry and that of half a grapefruit. Local tenderness is the most constant single sign.

This type of hernia is easily diagnosed and seldom missed unless reduction has occurred before examination. The cessation of symptoms upon reduction is positive proof that the hernia is the cause of the symptoms, and is the only actual therapeutic test for operation. Adherent

omentum is relatively frequent and calls for early operation. This is suspected when a hernia of more than average size is irreducible, tender, and produces visceral symptoms when pressed upon. However, most cases are not so well defined, and it is in the less evident type of epigastric hernia that the errors in diagnosis and treatment are most frequent. The usual history of such a case is that the patient has noticed the small lump years before, but that apart from tenderness on pressure it has given no symptoms. Or, again, the presence of the hernia was only discovered during the course of an abdominal examination.

At this point, mention should be made of the frequency of failure to diagnose epigastric hernia. The condition should always be borne in mind. It is discovered best by inspection with oblique lighting, careful palpation of the upper linea alba, first with the patient relaxed, and then with the recti tensed and the intra-abdominal pressure raised, as when the patient lifts his head and shoulders off the bed. Diastasis recti should not be confused. In obese subjects the hernial mass may be impalpable, but a definite single point of tenderness can always be found.

In the course of time symptoms develop which may or may not be due to the hernia. Friedenwald and Morrison report 65 patients operated upon of whom 28 owed their symptoms to various visceral conditions. In 158 operated upon for epigastric hernia at the Mayo Clinic, reported by Pemberton and Curry, 32 were proved to have other causes for the symptoms besides the hernia. In our series, where complete investigation was done prior to the operation or exploration done at operation, associated peptic ulcer was found in 8 cases, calculous cholecystitis in 1, chronic appendicitis in 3, carcinoma of the stomach in 1, partial intestinal obstruction in 1, nephroptosis in 1, and irritable colon in 1 case.

Again, the history of relief on lying down, or, conversely, aggravation of the symptoms by exertion or the upright position and relief by reduction of the mass, are strong presumptive evidence that the hernia is the cause of the symptoms. In the cases where visceral symptoms do result from an epigastric protrusion, the mechanism is probably a reflex one by way of the intercostal nerves to the corresponding splanchnic outflow going to the celiac ganglion.

The increased intra-abdominal tension causes a pinching of the hernial contents by increased tension of the fascial ring.

In order to determine the relationship of epigastric herniae to visceral symptoms an analysis was made of all cases of such a hernia repaired at the Mayo Clinic between 1910 and 1933. Of 296 cases, 158 were admitted solely because of the hernia, the cure of which it was hoped would relieve the patient's symptoms. Of these, 26 had an abdominal exploration at the time of repair, 11 being negative and 15 positive for visceral disease. The conditions found were divided between peptic ulcer, appendicitis, gall-bladder disease and partial obstruction. Thirty-seven patients had other herniae done at the same time, with relief of symptoms in 17 known cases; 95 had only the repair of the epigastric hernia done, of which 33 had no visceral symptoms, the complaint being only of the lump or local tenderness. The best final results occurred in this last sub-group, with 29 known cures. The worst results were in the group with visceral symptoms and only local repair of the hernia. Only 8 were cured, and these were aided by medical treatment; 34 continued to have the same symptoms as before operation; and 17 needed further surgical treatment for the discovery of definite visceral disease. Their statistics show that the best results are obtained in those cases with no visceral symptoms. When the latter are present there is no characteristic sign or symptom, local repair yielding poor results, with only 22 per cent relieved. Pemberton and Curry advise opening the abdominal cavity in all cases with visceral symptoms, even when pre-operative diagnostic measures have failed to reveal any evidence of organic disease.

Recurrences.—There is only one mention of recurrences in the literature and that is in the

last-mentioned series of Pemberton and Curry, who report 5 known recurrences in 158 cases, or 3.1 per cent. In our series there were 2 known recurrences in 33 operations, one of which recurred twice.

Treatment.—From a survey of our cases, and with the foregoing data from the literature, one is impressed by the high percentage of organic abdominal disease that is hidden by a diagnosis of epigastric hernia. How is one, then, to assess the value of such a rupture? The following points will, I believe, be of help in treating this rather ambiguous condition.

1. The strangulated or incarcerated types with a history coincident with the onset of the protrusion need little discussion. Operation is imperative as soon as possible, especially in the former variety.

2. Those with complaints of a lump in the epigastrium with local tenderness and no visceral complaints do not need investigation or exploration. Uniformly good results follow their repair.

3. Those cases most commonly seen in athletes or labourers, with a lump in the epigastrium following a definite strain or over-exertion, and in whom the symptoms, visceral or otherwise, disappear with the disappearance of the tumour will give good final results. This type almost always contains a sac which fills with a viscus (most commonly omentum) on assuming the erect posture. I do not believe that preliminary investigation or operative abdominal exploration is necessary in such a type.

4. The fourth group consists of those patients who seek medical aid for abdominal visceral symptoms, the hernia having been discovered previously by the patient or noticed for the first time during the ensuing physical examination. This group has as a rule only a preperitoneal fatty hernia with occasionally the inclusion of a small sac. What should be done in these cases? Too many doctors advise repair of the hernia as the first step, with the usually vain hope that the symptoms will be relieved. This procedure is to be condemned because of the small proportion of cures that result. There are two alternative procedures. The first and better one is a complete diagnostic investigation with emphasis on the gastro-intestinal tract, including the gall-bladder and pancreas, the renal tract, and the nervous system. Only if all tests are

SUMMARY OF CASES REVIEWED

Number of cases	46
Cases—male	42
Cases—female	4
Average age of patient	42.4 yrs.
Average duration of symptoms	5.2 yrs.
(Shortest, 2 days; longest, 40 years)	
Associated herniae of other varieties	10
Cases operated upon	33
Sac present in hernia	20
Preperitoneal fatty tissue	13
Omentum present in sac	7
(Reducible, 1; irreducible, 5; strangulated, 1)	
Operation without exploration or investigation	15
With pre-operative investigation without exploration	11
Abdomen explored (negative)	4
Abdomen explored (positive)	3
Associated conditions (abdominal lesions)....	16

negative is operation indicated, which may consist of repair of the hernia only, or, better still, combined with abdominal exploration, which often reveals lesions not shown by pre-operative investigation. If this pre-operative investigation is positive then medical or surgical treatment of the lesion found is carried out. The alternative procedure is exploration without pre-operative tests. This is not so satisfactory as the first procedure as the exploration is more haphazard and conditions other than surgical may be revealed. This alternative is only permissible when for some reason pre-operative investigation is impossible.

SUMMARY

1. The etiology, pathological anatomy and diagnosis of epigastric hernia are discussed.
2. An analysis of 46 cases of epigastric hernia is given, the outstanding feature of which is that 16 of them were found on investigation or exploration to be suffering from abdominal conditions other than the hernia.
3. The difficulty in assessing the significance of an epigastric hernia, particularly when associated with visceral symptoms, is stressed.
4. This type of hernia is divided into four groups according to the type and symptomatology, and a guide is given for the management of each.

POINTS OF MUTUAL INTEREST TO THE GENERAL PRACTITIONER AND THE RADIOLOGIST*

BY W. A. JONES

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THERE are many problems in the radiological field which, due to the overlapping interests of the general practitioner and the specialist, make the situation awkward and sometimes render it a little strained, often leaving the patient with a sense of bewilderment. Usually this is due to a misunderstanding of the situation and an unintentional lack of cooperation on the part of the two medical men involved. It is due in part, however, to the fact that the busy general man has not the time to keep himself informed of what is going on in the radiological world.

Generally speaking, the status of the radiologist should be that of a consultant, and his duty is to advise concerning diagnosis and treatment in his particular field. His methods of diagnosis may be complete in themselves, or, as often happens, are complementary to and serve to confirm clinical methods. Perhaps one of the great mistakes of our time is the tendency on the part of some men to expect the radiologist to hand out a typed diagnosis, reading the type as it were directly from the film and transferring it to paper as something turned out of a machine, mechanically correct, and purporting to be infallible. This view of what is to be expected of the radiologist is flattering but untrue.

While in many instances the radiologist is able to give a definite diagnosis, he is often only able to give impressions and opinions as to disease processes and function or lack of function of different organs, leaving the decision as to the diagnosis with the clinician.

Radiological diagnosis is, after all, another way of using "inspection" in the elucidation of the symptom-complex. One must not forget, however, that it is a particularly valuable method of inspection and is sometimes of more than ordinary use in the explanation of certain symptoms in which other methods may be indeterminate. One could recite at some length social and financial tragedies that have occurred due to late diagnosis of chest lesions and also of other diseases which might have been avoided if those who first saw the patients had used x-rays as a method of inspection along with their other methods of diagnosis.

While we are speaking of chests, it might be worth while to say something about the relative merits of radiographs and of fluoroscopy. Usually these two methods of x-ray examination are complementary, and very often both are required in order to arrive at a diagnosis. But there should be no shadow of doubt that the man who pronounces a suspected chest free of incipient tuberculous disease on the screen examination alone is flirting with disaster and is

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unfair to his patient. A film or films of excellent technical quality are required, and if such quality is not attained at the first trial they should be repeated. It should be remembered, however, that although the x-ray film will not infrequently show manifest tuberculous lesions before they can be picked up by other methods of examination it is not infallible, and incipient disease may exist and not be demonstrable on the film. Therefore, the making of a film does not make less necessary the need for careful clinical examination of the patient.

The question of the use of fluoroscopy in examination of the gastro-intestinal tract also arises. Many a radiologist has raved inwardly and torn his hair, at least figuratively, when there arrives in the mail a host of films, made of the stomach or colon of a patient. Sometimes, of course, the diagnosis is self-evident on the films, but usually this is not so. The reason for this annoyance on the part of the radiologist is that the radiologist knows that he depends as much or more upon the screen examination as he does upon the films. He knows that these innocent looking films may conceal behind the barium shadows niches and filling defects that are diagnostic of disease, and that the only way to be sure of these things is to screen the patient. And, therefore, because he can only give a reading of the films, he is not satisfied that the work has been properly done. It is true, of course, that the film is needed to show fine details when these are demonstrable and also to make a record of any pathological condition that may be found.

In this association one would like to make a plea for the complete examination of the patient who is sent for investigation of stomach symptoms. Too often the radiologist is asked to examine the stomach only, as the symptoms are said to point to nothing else. This is equivalent to sending the patient to the internist and asking him to examine the head only, because the patient's chief symptom is headache. I am firmly convinced that, unless a definite lesion is found in the stomach or duodenum at the examination of these parts, the whole gastro-intestinal tract should be investigated, and that usually an examination of the gall bladder should be carried out. If all these organs are negative, then one should remember that lesions of the kidneys and ureters are not unrelated to stomach symptoms, and might be included in the examination.

One would also like to plead for time in conducting an examination. Too often the patient is impatient, and the doctor expects the impossible, and, in an endeavour to please both, blunders may be made. Too often the patient, who has had symptoms for five years, wants a complete investigation in a period of as many hours. It is quite true that at times the diagnosis may be evident five minutes after the examination is commenced, but so often it takes as many days to arrive at a diagnosis. In this connection one should also mention the need for proper preparation of the patient, such as, the necessity for an empty stomach before a barium meal is given, the need for proper preparatory purging and administration of the dye for the gall-bladder case, and the administration of at least two to two-and-one-half ounces of castor oil the night before, to cleanse the colon satisfactorily before giving a barium enema.

Too much reliance should not be placed upon the fluoroscopic diagnosis of fractures. The fluoroscope is an excellent medium to aid in the adjustment of the fragments when the fracture is being set, but it should be noted that when the fracture line is indistinct and there is practically no displacement of the fragments the diagnosis may be missed, and an erroneous conclusion reached unless films are made. Strangely enough, it is these very cases with doubtful fractures that the radiologist is asked to screen "because there probably isn't a fracture present". This may be a costly mistake and more than one man has come to grief over such an error in the past.

After a fracture has been set or a dislocation reduced invariably a film record of the event should be made, not only to satisfy the practitioner that all is well but also that proof of such can be produced at a later date. The Canadian Medical Protective Association has warned its members more than once regarding the need for this. It is quite as necessary to have films made after the setting of the fracture as it is before, and neglect of this precaution may cause the practitioner a considerable degree of embarrassment if he should be called upon to defend himself in the court room.

Before we leave the question of radiography and fluoroscopy it would perhaps be wise to spend a few minutes in discussing the danger of radiation dermatitis and ulceration and the

means of protecting the patient and the practitioner from these effects.

Skin reaction to radiation may show itself in either the acute or chronic form. In the acute form it is the result of a relatively massive dose of irradiation delivered within a comparatively short period, and manifests itself by a skin response much like that of a sunburn in its primary stages. Unlike sunburn, however, it does not show an erythema until several days to a couple of weeks after exposure. If the dose has been too heavy it eventually results in a chronic painful ulcer that takes years to heal or may never heal. The ulcer and also the damaged skin are prone to malignant change in later years. A skin reaction of this type that heals without ulceration may show itself some years later in a similar manner to the skin changes that take place in the chronic form.

In the chronic form the skin reaction is the result of repeated minor doses of irradiation over a period of months or years and shows itself by evidence of skin atrophy, telangiectasis and papillomata which eventually may become malignant. The acute form is the type that the patient is most likely to get as a result of prolonged and improper x-ray examination, while the chronic form is usually reserved for the practitioner who receives x-ray exposure on the hands over a period of months or years.

The patient is protected by being sure that filtration is present to screen out the softer x-rays, that too many films or too prolonged screenings are avoided, and by not repeating lengthy examinations until at least a period of one month has elapsed. In addition to this, in screening, the aperture through which the rays pass is diaphragmed down to the smallest size consistent with the examination. When searching for foreign bodies it is well to have a timer on the fluoroscope that will cut the x-rays off, before the danger point of over-exposure is reached. The intensity of the x-rays should also be kept down to the lowest limit consistent with proper visualization of the foreign body. The reason for this is that foreign bodies are sometimes so evasive that the search for them goes on for longer than one anticipates, and there is great danger of over-exposure.

With regard to the practitioner, he must of course protect himself against a massive dose in a similar way to that which is used for the protection of the patient, but in addition, if he

would avoid a chronic dermatitis, he must be consistent in avoiding even small amounts of exposure at all times, because if he is doing much fracture work under the screen or searching for foreign bodies, the effects of the rays are cumulative and may effect him after months or years of exposure. He should keep his hands out of the direct path of the rays, and use the rays as little as possible during the examination of the patient. He will thus avoid the unpleasant results that have happened to too many men who have suffered in the past. Radiologists suffered from this chronic form previously, but they have learned to protect themselves in a large measure. It now appears to be the turn of the general practitioner and surgeon who do much fracture work under the screen to protect themselves in a similar manner.

It is in the field of radiotherapy that the relationship of the radiologist to the practitioner changes somewhat. Here, we no longer have a patient referred for a comparatively short time for purposes of examination and of consultation, because it may become necessary for the radiologist to give treatment over a period of several weeks, and in malignant disease to continue supervision of the patient over months or years. It is here that the need for mutual trust on the part of the radiologist and the general practitioner becomes vitally necessary. There should be the closest cooperation and the broadest degree of tolerance to allow for words spoken in the exigency of the moment. It is a situation not devoid of pitfalls for those who are touchy and prone to professional jealousy, and a spirit of mutual trust and frankness is best for all concerned. One might remember that in our Code of Ethics the idiosyncrasies of the patient are considered, and we are told that "reasonable allowance should be made for the mental infirmities and caprices of the sick".

The medical practitioner, having once decided that he is going to turn his patient over to the radiologist for treatment, should allow him to be the judge of how and when that treatment is to be administered. If there are times when he, as a practitioner, considers that it is in the patient's interest that treatment be discontinued or modified, he should consult with his confrère and be guided in this particular by him. Too often it has been the experience of the radiologist to have several days of treatment utterly wasted and the chance of a successful result

entirely lost due to an unguarded statement made to the patient by his medical attendant. Many difficulties arise owing to a lack of understanding of the fundamentals involved in treatment. It is with the idea of meeting some of these problems that I wish to describe a few of the principles involved in radiation therapy.

Radiotherapy may be used to advantage in the treatment of many skin disorders and in inflammatory lesions of various kinds, but it is particularly to the treatment of tumours, both benign and malignant, and of allied conditions that your attention is now directed.

Radiotherapy depends for its results on the difference in the sensitivity of various kinds of cells. Those cells which more nearly approach the embryonal type are relatively the most radiosensitive and succumb most easily to the effects of radiation. Those types of tumours which grow most rapidly are usually radiosensitive. In addition to the direct lethal effect upon the malignant cells by the rays, there is also an effect upon the stroma, the sequelæ of irradiation being sclerosis of blood vessels and the formation of tissue fibrosis, the cells being deprived partially of their blood supply and many becoming enmeshed in fibrous tissue.

X-rays and radium have practically the same effect upon tissue, and they are used independently or combined according to the site, the accessibility, and the environment of the lesion. Radium is used in the uterus, lip and tongue, and upon the skin, and is often combined with x-rays in these regions. So-called "deep" x-rays are usually used for deep-seated lesions, but occasionally they are used in the treatment of surface lesions, for example, in the treatment of malignant skin lesions that have involved bone and cartilage. In this connection it is of value to note that when the practitioner is discussing the possibility of radiation treatment with the patient he would do well to speak in general terms. He should not specify that radium or x-rays will be used, because when the patient consults the radiologist and the opposite mode of attack is instituted the patient then inclines either to lose faith in his or her medical attendant or to doubt the wisdom of the radiologist.

A problem of vital interest is the question of the reaction of the skin and mucous membranes to irradiation. The patient suffers somewhat from physical discomfort, which is distressful

more or less according to his nervous makeup. He will also suffer mental discomfort or actual mental distress if the skin reaction is referred to as a "burn". The word "burn" in association with radium or x-ray treatment produces in the patient's mind a chain of ideas which is sometimes terrifying. Therefore, it should not be used in this connection, but should be reserved for cases of actual chronic ulceration produced directly by irradiation.

The physiological course of the reaction will vary somewhat according to whether the irradiation has been given as a massive dose or has been fractionated. If given as a massive dose there may be a primary reaction coming on within a few hours, which shows as a puffiness of the subcutaneous tissues, and, more rarely, this is accompanied by a blush over the skin surface. This subsides within a day or so. After about ten days or two weeks the skin begins to turn pink, and as each day passes this pink becomes more intense until the skin finally is bright red in shade and later may even turn a purplish red colour. The reaction usually reaches its height about the end of the third week, and at this time, if the reaction is severe enough, the skin may be blistered and exude serum. Over a period of some three or four weeks the skin gradually becomes more normal in appearance, and at the end of six or eight weeks the reaction has quite disappeared, leaving the skin pale or almost normal in colour. At times, when blistering does not occur, the skin becomes deeply tanned, and this may persist for several months. During the period of heavy reaction the patient may experience much discomfort. In some patients this is quite marked and may require the administration of aspirin, phenacetine and caffeine, and at times codeine. The application of 1 per cent carbolic ointment is sometimes useful and nupercaine ointment may be used with benefit. Butesin picate ointment often alleviates the smarting of the skin, but unfortunately a number of people are sensitive to it, and when used by such a spreading dermatitis results. The spread is due to the fact that the patients believe the dermatitis is radiation reaction, and they pursue this "reaction" farther and farther afield with the butesin picate in an endeavour to catch up with it. I have seen a patient with a small area on the nose, about the size of a quarter, of actual radiation reaction, reappear at the clinic with

a chemical dermatitis that included both ears and was spreading down the back of the neck.

The mucous membrane turns grey when reacting, and the reaction takes place earlier than in the case of the skin.

It is necessary to keep the reacting skin clean and it should be bathed with warm boracic solution two or three times daily, followed by the application of vaseline or other bland ointment. A mixture of zinc oxide and castor oil is also a useful dressing. The part must be kept clean to prevent the formation of a scab.

When radiation is given by the fractionated method the total dose is much more than when the massive dose method is employed. The reaction of the skin is also a little different from that reaction which develops when the total dose is administered at one time. The method of giving this treatment is to administer daily a radiation dose equivalent to about $1/8$ or $1/5$ of what would be administered if a single massive dose was given. There are many variations of this, and, depending upon the amount of daily dosage given, the fractionated method of treatment may extend over a period of several days or several weeks. The advantage that is claimed from this method of treatment is that it is more selective and does more damage relatively to the malignant cells than to the cells of normal tissue. Usually the radiation continues to be given even after the skin has already commenced to react, and experience is the guide which largely determines when the dosage has reached the limits which gives the optimum biological reaction.

One often hears the question of dosage discussed and such is often laid down as being so many "r" units. It must be said that there is no standard dosage for radiation therapy. There is a standard unit of measurement known as the r unit. This is a useful unit for measuring dosage, and, if one might, as Richards has done, draw an analogy to the dosage of tincture digitalis given the cardiac patient one might think of the r unit in the same manner that one thinks of a minim of the tincture. Similarly, the total dosage must be considered as an equivalent of the biological response of the patient, the tumour and the skin or mucous membrane, just as one gauges the total dose of tincture of digitalis by the clinical reaction of the patient. It is only the study of the patient's reactions and the nice

adjustment of dosage to reaction, as dictated by experience, that give results in radiation therapy of cancer. An endeavour to work out a series of treatments by mathematical formulæ alone is doomed to failure. It is the realization of this fact which is improving constantly the results of radiotherapy.

I would like to state at this point that the application of radiotherapy as administered generally today is so different from the type of radiation treatment given as short a time ago as five years, or even less, that statistics collected of work done previous to that time cannot be looked upon as establishing a standard of what may be expected with present methods.

There is not time for discussion of the problem of whether or not pre-operative irradiation is useful, but Dr. James Ewing, an internationally known pathologist, who has had a considerable degree of experience with this method of treatment states that he is satisfied that the type of fractionated deep x-ray dosage which his associates carry out as a preliminary to surgery, followed by surgery in two months, gives the patient the best chance of recovery from cancer of the breast.

The criticism is frequently levelled at radiation therapy that it often fails, that it often destroys normal tissue, and sometimes it has been said by those who have not been fortunate enough to see the good results, that it is only palliative. All of this is disconcerting to the general practitioner because these statements are often made by men who are outstanding members of the medical profession. Indeed it happens once in a while that the practitioner himself has had the experience that the half-dozen cases he has sent for radiotherapy have not done well. With regard to the last point, surely anyone who has read the medical literature of the last few years cannot fail to be impressed with the marked usefulness of radiation therapy in malignant disease. A review of the papers published in the *Canadian Medical Association Journal* for 1937 and many other medical and surgical journals should quite thoroughly establish this point. That it often fails to cure is quite true, and there is certainly room for some method of treatment in addition to surgery which may eventually replace or supplement irradiation. One should remember, however, that many cases that might have been

benefited or cured in the early stages arrive for irradiation in an already advanced and hopeless state.

Does irradiation often destroy normal tissues? Of course it does. It always modifies normal tissue when used to treat malignant disease, and the further advanced the disease is, the heavier and more widespread the radiation must be, and finally we reach a point when, in order to exterminate the malignant lesion, normal tissue must be destroyed. But is this not perfectly justifiable? Does not the surgeon amputate limbs and remove organs if such become necessary to save the patient's life? Does he not justifiably disfigure patients when the necessity arises? How much more so is the radiologist justified in doing likewise when it is remembered that the cases sent to him, which suffer in this way are, in the main, beyond the help of surgery.

One of the problems of radiation therapy is that of the necessity which sometimes arises of irradiating a lesion which recurs in a previously irradiated area. When this happens one must balance the danger of radiation necrosis and the possibility of a successful result against the patient's life, well knowing that disaster may follow under any circumstance. Frank acceptance of the possibility of irradiation ulceration by the patient and the medical attendant makes the choice of treatment easier.

After an operative procedure has taken place and there is recurrence of a malignant lesion close to the scar of the incision there is every likelihood of the breaking down of the scar tissue if sufficient radiation is given to destroy the lesion. This sometimes happens at the time of the radiation reaction and at times some weeks after. In any event it is unavoidable and should not cause grave concern, as the lesion usually heals in a few weeks' time.

Before closing I would like to make a plea for the proper interpretation of the reaction following irradiation. Like vaccination, irradiation is also plagued by being blamed for all ills that may follow thereafter. The symptoms of unfavourable progress of the malignant lesion itself, skin recurrences of the erythematoid type, ulceration due to the disease, herpes and other complicating conditions, and even death due to other causes have all been ascribed to the effect of irradiation. It is often blamed for metastases. Strangely enough, medical men themselves often leave such impressions with the patient. Sometimes this is done with the idea of beneficently deceiving the patient with regard to the true status of the case; at other times one wonders why it is done. The pernicious effect of this error however is that it discourages others, terrifies some, and prevents the use of a beneficial method of treatment by a number who need it.

THE PSYCHIATRIST'S POINT OF VIEW*

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IT is likely that the psychiatrist, more than any other medical specialist, experiences difficulty in analyzing, accepting and retaining the basic postulates of his science. In his special field he must take into account the day by day behaviour of his patients as well as the functioning of their various organs. For patients are living persons as well as medical "cases". They have feelings and attitudes, friends and families, occupational and recreational pursuits

which must be evaluated as factors having possible importance in diagnosis and treatment. Difficulties arise when the psychiatrist endeavours to find some systematic point of view which will reconcile the traditional medical approach with sociological and psychological methods. It is the purpose of this paper to review some of these difficulties.

During the early stages of his medical training the future psychiatrist is not recognizably different from other students. He is usually conscientious and willing to undergo the many years of study which are necessary if he is to earn his living in any specialty. He is somewhat of an idealist, and is eager to do some

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good in the world. He may be genuinely interested in religion. With other students he begins on the long trail towards knowledge of that peculiar mass of thinking, feeling and acting protoplasm—the living human. In his pre-medical work or in his first year in medicine he takes lectures and laboratory courses in the fundamental sciences—physics, chemistry and biology. It is at first difficult for him to see what these studies have to do with curing sickness. They seem to be totally unrelated to his preconceived ideas of medicine, and often they appear to be quite unrelated to each other. It must be admitted that the content of such courses is too often determined by mere pedagogical convenience, rather than by such foresight as would integrate the various disciplines one with another.

The basic medical sciences, anatomy, biochemistry and physiology, seem to be more to the point. Here, at least, there is an apparent relationship to man; and, superficially at any rate, there is a rational interrelation between the disciplines. By implication as well as by direct teaching the student begins to visualize man as a sort of machine. In the biochemistry class living activity is thought of in terms of chemical change and interchange; in anatomy it is a question of muscular and skeletal action; in physiology it is conceived in terms of organ-function and the controlling effect of the central nervous system. Remarkably little time is spent in helping the student to grasp the essential unity of these apparently divergent points of view. Only rarely is there a special course which systematically interrelates the disparate facts, and which thus leads to an understanding of man as an individual, both influencing and being influenced by his environment. How this human machine functions, why man behaves as he does—these and similar questions are answered in terms of neurophysiology only. The gastrocnemius muscle of the frog can be made to twitch vigorously when a stimulus such as a mild electric shock is applied to the end of the attached nerve. There seems to be only a small step from this simple and easily understood fact to the complete explanation of human behaviour in terms of neuro-muscular mechanisms. What happens to the student's moral ideals and religious concepts? There is not much room for moral principles and ideals in a machine, no matter

how complex it is. There is certainly no room for a soul.

In the clinical years the student sees human beings suffering from diseases of various kinds. The theories of the cause and cure of disease are still, on the whole, quite coldly mechanical. Disease implies pathology—disordered function through damaged cells. If no lesion can be found it is because our science is not yet far enough advanced. Eventually, it is assumed, the pathology will be known. Treatment is directed to the cause of the trouble when this is known. Medicines and other therapeutic devices are used, with the idea of correcting the “etiological factors”. Occasionally the older clinicians will talk of the importance of treating the patient as a whole. The student, however, often loses sight of this idea in his enthusiasm for an “interesting case of diabetes”, or a “difficult operation on a deformed hip”. He is too busy reading texts and measuring cardiac dullness to worry much about the sick and suffering human being.

After he has graduated the student is all too apt to have an enlarged opinion of his own scientific training and equipment. His philosophy of life has become less idealistic, if not frankly materialistic. For him, disease is the direct mechanical effect of definite antecedent causes and health is, as a rule, simply the *absence of disease*. The unfortunate result of this preliminary medical training is that, frequently, the future psychiatrist is unaware of the many other ways of studying man.

In recent years, as an attempt to remedy this state of affairs, courses in psychology have occasionally been added to the curricula of medical schools. The danger of this procedure is that, instead of integrating the various courses of the curriculum, it may merely add an extra subject for the overworked student. It is as if another patch were added to a patchwork quilt in an effort to blend together the whole design. A sound course in psychology can do much to train the student to recognize and evaluate the various fundamental assumptions made in the study of man. But this is not enough. It is essential that *all* of the fundamental pre-clinical subjects be so integrated that they may lead to an understanding of the normal human being functioning as a whole. Psychology can help in this but it cannot do the whole job by itself.

About a year ago an important university in England appointed a committee to decide whether psychology should be added to the curriculum of its faculty of medicine. The idea was finally voted down because it was held that there were so many different schools of psychology and so many conflicting points of view that the medical student would never have time to become acquainted with all of them. Moreover, the committee could not agree in selecting any one approach. Surely it would be a very good thing for medical students to become acquainted with the various ways of viewing the same facts, and to realize as clearly as possible the limitations of each point of view? A carefully prepared course in psychology could do this without overloading the curriculum unduly. The importance of this training, especially for the neuropsychiatrist, will become increasingly evident.

To return to the discussion of the usual development of the psychiatrist. It is not until the young doctor has completed a year or two as an intern in a general hospital that the question of a specialty arises. Let us suppose he chooses psychiatry. It is assumed that he is genuinely interested in this field, and is not merely looking for a job. The moment he starts dealing with those who are "mentally ill", he finds that he must study subjective as well as objective phenomena. The thinking, feeling and acting of his patients must not only be objectively observed but also subjectively understood. The concept of *the whole man*, reacting and adjusting to personal difficulties and environmental obstacles, becomes increasingly meaningful. The mechanistic concept of disease is still present, but is limited in its usefulness. Such non-materialistic phenomena as "personality deviations", "disturbances in thought", and "affect-disorders" must be taken into consideration along with the more familiar pains and aches of disease. The student may even meet some psychiatric authorities who talk quite confidently of thought transference, the science of the occult, and the existence of a soul!^{1, 2, 3}

Sooner or later the student of psychiatry will naturally turn to psychology. Some systematic knowledge of "mental" activity as observed in normal persons, as well as in his patients, is essential. By and large, the particular brand of psychology that is used in psychiatric prac-

tice is "hormic". It is *teleological* rather than *mechanistic*. Instead of being considered as a machine put into action with mechanical precision by antecedent stimuli which, trigger-like, produce responses, man is thought of as being motivated by some urge, drive or life impulse, which draws him on to some future goal. In hormic psychology the lines of force are conceived as pulling from ahead toward this desired goal, rather than pushing from behind in the form of mechanical stimulation. Hormic psychology is therefore definitely purposive. The urge to achieve some desired end may be a conscious one, as in the case of a person hurrying to catch a street car, or a totally unwitting one, as in the case of the neurotic's "retreat" into illness. This psychology, therefore, has a place for the fundamental *instincts*, which are the motivating drives, and for *conflicts*, which arise when these drives clash with one another or with social customs and taboos. Disease then becomes not so much the result of mechanical change as a new form of behaviour emerging through the effort of the individual to adjust himself to the situation created by this conflict. Thus even disease seems to be purposive.

It is important to understand that, while it makes no difference scientifically which of the two points of view be adopted, *they cannot both be used at the same time*. Mechanism and teleology are mutually exclusive. Each is important in special fields however. The physiologist works more satisfactorily with a mechanistic point of view, while the psychiatrist, in the present state of his science, usually finds the teleological approach more helpful. He can understand more of the phenomena he observes if they are fitted into such a psychological scheme. Nevertheless, it is astonishing how many psychiatrists-in-training do not realize that there is any conflict between their old "scientific" mechanism and their new implicitly accepted teleology.

As the young doctor progresses farther in his studies he begins to realize that there are many conflicting schools of psychology all classed as hormic and teleological. He reads of McDougall, Hart, Jung, Adler, and, most important of all, Freud. The Freudian or psychoanalytical psychology has an extensive literature and a large number of "sectarians" who are continually making it even more ex-

tensive. The young psychiatrist, especially if he has not been trained in the fundamentals of academic psychology, is almost certain to be impressed by the apparent logic of psycho-analytic doctrine, and by the spectacular interpretations of human behaviour to which it leads. The great danger is that the student may accept uncritically this or some other "school" without being familiar with the implications of that acceptance. Perhaps he may react in just the opposite way. After a hasty perusal of some of the psychological concepts in current use he may reject the whole thing as being utterly fantastic and absurd. As a scientist interested in the study of human behaviour he should realize that these psychologies, once the first basic postulate of a "purposive biologic urge" is granted, are usually quite consistent. Scientific criticism should not be directed at the teleology, which is no more of an assumption than mechanism. Criticism can and should be levelled, however, at any logical inconsistency which is apparent after granting the basic postulate.⁴ It should throw the searchlight on any suggestion of mysticism or cultism and on the use of far-fetched analogy as proof of an hypothesis.

During his post-graduate work the young psychiatrist will usually take some special training in neurology. Here, at one fell swoop he is plunged again into the old familiar physiological mechanism. Once more it is man, the machine—not man, the instinct-motivated person. Disease once more is a matter of cell damage; and diagnosis becomes a problem of locating the damage by means of clinical tests. The analogy of a linesman locating trouble somewhere in a tangled mass of telephone wires is freely used. Behaviour is a function of the cortical and sub-cortical layers of the brain, and temperament has to do with the basic ganglia. Increasing emphasis is placed on exact cortical localization.

What is the upshot of all this apparent confusion among conflicting disciplines? At present there is no one solution to the problem that is acceptable to all. On the contrary, the attempts at reconciling the basic disciplines in a logical and scientific manner have been remarkably varied. For some doctors the problem simply does not exist, because the basic assumptions are not clearly understood. For many others the solution involves a kind

of eclecticism, either implied or frankly acknowledged. While there is much to be said in favour of an eclectic point of view, it would nevertheless seem desirable that physicians should know why and when they are being eclectic.

Often the practical psychiatrist or neurologist boasts that he "takes his facts as he finds them", and that any concept, if useful to him in his task of helping people, is acceptable, no matter what its origin. He is an *intuitive-eclectic*. He is not interested in discussions about the origins of his concepts. Such "arm-chair psychologizing" makes him impatient. If questioned, he usually states that he is an advocate of no particular school, and that he always keeps to the "middle of the road". Yet it is hard to imagine this road when no warning sign-posts or even delimiting ditches or fences are recognized. The system of psychiatry presented by Sadler is an excellent illustration of "intuitive eclecticism".

In recent years psychiatrists have been trying to make eclecticism a little more systematic. Adolph Meyer, in America, and Mapother, in England, are two leaders of such attempts. Dissatisfied with the intuitive and uncritical sort of eclecticism practised in their specialty, they have endeavoured to work out a pragmatic point of view which would be both logical and scientific. Their separate efforts have produced *psychobiology*⁶ and *nominalism*,⁷ respectively. Both were interested in phenomena as observed, and both tried to avoid any scheme for the conceptualizing of phenomena by means of hypotheses or theories. Any fact having its basis in reality was acceptable as a phenomenon, and the definition of a fact was "anything that makes a difference". Nominalism has been claimed by many previous psychologies, including the mechanistic psychology of behaviourism and the teleological psychology of such psychiatrists as Gillespie, Ebaugh and Strecker. Psychobiology, in addition to its nominalistic background, stressed the all-important fact that man must be studied as a whole, as "a functioning unit in a changing and changeable environment". Just as blood pressure is a function of the circulatory system (and therefore an essential part-function of man), so personality is a function of man as a whole. Even the function of the brain and nervous system must be considered as a *part-function*, and must not be confused

with the more important *whole-function*. The various part-functions are studied in order to gain an understanding of the whole. There is no difficulty in deciding which is more important—body or mind—or in understanding the relationship existing between these two. Both have part-functions in the function of the whole. In psychobiology, then, we have a point of view that, to a degree, satisfies the needs of both the medical student and psychiatrist. It stresses the integration and the correlation of all of the known facts concerning the functioning of the human individual. Because it insists on accepting useful ideas coming from any quarter it is eclectic. It avoids conflict with any system of psychology or any logical formulation of scientific ideas by refusing to be conceptualized into any logical system.

If any criticism can be levelled at psychobiology and its fundamental nominalism it must be directed at this one weakness. It avoids coming to grips with basic assumptions simply because it completely ignores them. Mechanism and telology are thus not reconciled in any sense. They remain as before, except that the psychobiologist, in his effort to use only the "facts", adopts first one point of view and then the other. He is teleological when he speaks of the individual "adjusting to a life-situation" or "reacting to his unconscious determinisms"; he is mechanistic when he speaks of the "impairment of function through senile changes in the brain and throughout the body." He insists there is no use explaining the difference between body and mind; and then proceeds therapeutically as if there were all the difference in the world between them. Such eclecticism, steering clear of any contact with systematic formulation, places its emphasis on the person who is being examined. It is the patient who is considered from the various points of view of his part-functions. In the clinical situation, for example, the patient is examined physically. Then an effort is made to survey the various influences of his environment, his social and emotional development as well as his present mental status. The facts thus collected are integrated only by the fact that they all have to do with one person. It is somewhat like an attempt to gain an understanding of the culture of a race of people by collecting data on everything

imaginable having even a remote connection with the people or their country. The really significant data may or may not be collected by this method. But it would be much more to the point to begin the collection of data with some particular point of view or frame of reference in mind. Scientific method demands a certain limitation of the field in which we are to work. The limits of this field may be narrow or broad, depending on the purpose in mind, and they may be changed as the study progresses. But they must not become so broad in scope as to be meaningless. The frame of reference or point of view from which facts are considered is closely related to hypothesis and theory. Just as we must limit the field to prevent too wide a dissipation of effort we must also have some working hypothesis continually before us, in order to give us at least a tentative interpretation of the data we collect, and to suggest the direction of further search for additional facts. It is needless to emphasize that the hypothesis should never be hard and fast. Like the limits of the field it must be easily changeable; and we must be objective enough to see when it needs to be changed. It is a useful servant but a difficult and inhibiting master.

For these reasons the following point of view is suggested for the consideration of the psychiatrist. It is not exactly a new point of view, but it might lead to one. Assuming that the very nature of our selected field—the behaviour of the whole man, his personality, his thinking, feeling and acting as well as his physiological functioning—demands an eclectic point of view, is there any way in which we can make this eclecticism a little more systematic? The field of study is dangerously broad. We must narrow it if we are to work effectively. Although, as clinicians, we are concerned with the whole man, practically we can only consider one aspect of him at a time. In other words we must select arbitrarily one limited field of study at a time—and this field (set of facts) will be viewed in terms of a temporarily assumed point of view. We will quite deliberately put on suitably coloured spectacles through which the data or set of facts collected can be regarded. These spectacles may give a mechanistic appearance to the data or they may be any one of the many teleological varieties. The point is this, *we always know*

what spectacles we are wearing, and we can change them at will, whenever it seems necessary or desirable. The medical student had to change spectacles every hour or so during his undergraduate instruction. Although he seldom realized it, every different subject implied some shift in point of view. It is suggested that these changes in point of view should be fully recognized for what they are, and that the various kinds of frames of reference should become quite familiar to the doctor in training. The psychiatrist and neuropsychiatrist, particularly, should be adept at changing from one frame to another, recognizing, of course, that no two frames of reference are tenable at the same time.

The difference between this *rational eclecticism* and the other forms of eclecticism, including nominalism and psychobiology, is at once apparent. While rational eclectics deliberately assume the spectacles of any desired point of view, the other eclectics prefer to view the data without any spectacles at all. While it is conceivable that the latter method might give a clear and unbiased picture of the facts, is it not also possible that the same facts would become more sharply defined and more meaningful when spectacles are used? This is especially true if we do not rule out the possibility of taking off our spectacles altogether when they are no longer useful. We do not

quarrel with psychobiology any more than we do with psychoanalysis or behaviourism. But we are continually on the lookout for the limitations of each of these if used as an exclusive approach to psychiatric problems.

To change spectacles is admittedly more difficult than to adopt one kind of spectacles only, and force every fact, willy nilly, into one system of interpretation, or to go without spectacles altogether. But in terms of clear scientific thinking it is at least worthwhile to know when spectacles are being worn. Only in this way will we avoid both the false security of the sectarian and cultist and the inhibiting effect of unimaginative nominalism. It is hoped that, given familiarity with many different points of view, the psychiatrist will eventually find a new and more useful frame of reference emerging—one that, while in no sense reconciling conflicting hypotheses, will enable the relationships between data to be more clearly envisaged and result in a better understanding of man.

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ON THE VALUE OF CORRECTING THE RED CELL SEDIMENTATION RATE FOR THE EFFECT OF CELL VOLUME*

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NUMEROUS authors have shown that the sedimentation rate of erythrocytes is markedly influenced by *in vitro* changes in the concentration of red cells. It has been assumed by several authors that *in vivo* cell volume changes, anæmia and polycythæmia, exert the same effect, and that on this account the observed sedimentation rate should be corrected for the effects of cell volume. Methods to effect this correction were devised by Gram,¹ Rourke and Ernstene,² Walton³ and others, and the clinical data presented by these workers^{4, 5, 6} lead them to believe that the corrected sedimentation rates (C.S.R.'s)

offer more valuable data than do uncorrected sedimentation rates. Other authors, to whom reference will be made later, have arrived at the opposite conclusion and find that correction for cell volume introduces greater errors than it eliminates.

The purpose of this paper is to compare the relative value of corrected and uncorrected sedimentation rates, as found in 1,800 sedimentation tests upon approximately 800 patients in this tuberculosis sanatorium. It is well known that in tuberculosis there is usually a good correlation between the sedimentation rate and the clinical condition of the patient, so that the data presented herewith should be of value in decid-

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ing whether or not it is desirable to correct the observed rate for the effect of cell volume. With most patients no great difference was found between the uncorrected and the corrected rates; such cases offered no data upon the desirability of correcting for cell volume. Of the 1,800 tests, 1,619 were excluded from more detailed examination on this account. The remaining 181 cases were reviewed in detail by one of us (D.W.C.) as regards clinical evidence and x-ray findings, and a decision was made in each case as to whether the uncorrected or the corrected rate was in accord with the clinical data. In 94 of these cases, or 52 per cent, the uncorrected rate was found to be more satisfactory than the corrected rate, while the reverse was true in 87 cases, or 48 per cent.

TABLE I.

DISTRIBUTION OF 181 CASES BY PERCENTAGE OF NORMAL CELL VOLUME, INDICATING WHETHER THE OBSERVED OR CORRECTED RATES CONFORM TO CLINICAL DATA.

Percentage of normal cell volume	32	60-70	70-80	80-95	105-120	120-125
Corrected S.R. better than observed S.R.	0	4	12	30	40	1
Observed S.R. better than corrected S.R.	1	9	28	35	20	1
Total	1	13	40	65	60	2

The grouping of these results is indicated in Table I. For convenience, the groups are expressed in percentage of normal cell volume, 42.5 c.c. of packed red cells per 100 c.c. of blood being taken as normal, this being from Gram's figures the mean of the average cell volumes for men and women. Correction for cell volume was made by the method of Hambleton and Christianson.¹⁰

In one case of marked anæmia, of 32 per cent cell volume, the observed sedimentation rate was the better. For 13 cases of 60 to 70 per cent cell volume, the observed rate was the better in 9 cases, and the corrected rate in 4 cases. For each group below 95 per cent cell volume it was found that the observed sedimentation rate gave accurate results more frequently than did the corrected sedimentation rate. Altogether there were 118 cases having less than 100 per cent cell volume; of these the observed rate was the better in 72 cases, or 61 per cent, the corrected rate in 46 cases, or 39 per cent. Hence for all degrees of anæmia these figures indicate that correction for the effects

of cell volume is in general to be avoided. On the other hand, in patients having over 100 per cent cell volume the observed rate was better in 21 tests, the corrected rate in 41 tests. According to these findings, correction for cell volume should be of value with patients having over 100 per cent cell volume.

TABLE II.

AVERAGE SEDIMENTATION RATE IN EACH GROUP. FIGURES ARE NOT GIVEN WHERE ONLY ONE TEST FALLS INTO A GROUP.

Percentage of normal cell volume	60-70	70-80	80-95	105-120
Corrected S.R. better than observed S.R.	60	40	30	10
Observed S.R. better than corrected S.R.	39	39	28	17

In Table II is given for each group the average uncorrected sedimentation rate. In those blood samples which have 70 to 95 per cent cell volume the average one-hour sedimentation rate is about the same, regardless of whether the observed or the corrected rate is in better agreement with clinical findings. For samples containing 105 to 120 per cent cell volume, where the corrected rate is the better result, the average one-hour sedimentation (uncorrected) is 10 mm., *i.e.*, these are slow-settling bloods. For samples within the same cell volume range, where the uncorrected rate is the better, the average one-hour sedimentation is 17 mm. In other words, correction for cell volume is in general of advantage only for a limited number of blood samples, those having a high cell volume and a low sedimentation rate.

Correction for cell volume often leads to absurd results when applied to cases of marked anæmia or polycythæmia. For example, the patient having only 32 per cent cell volume had an observed sedimentation rate of 68 mm.; corrected for cell volume, this would come, as closely as we can estimate, to 7 mm., a normal rate. Yet this patient, a young man, died a month later with extensive pulmonary and intestinal tuberculosis. In another case which is not included in this series a patient with marked polycythæmia, approximately 8 million red cells per c.mm., had an observed sedimentation of 1 mm. Due to recurrent intestinal hæmorrhages, this patient's red cell count fell at times to less than 5 millions, yet his sedimentation rate remained unchanged at 1 mm.

Hence *in vivo* changes in cell volume do not necessarily affect the sedimentation rate. In serial sedimentations upon the same patient it was observed at times that, while the observed sedimentation rate varied little, changes in the patient's cell volume caused the corrected sedimentation rate to show larger fluctuations, and these were not in accord with the relatively unchanged condition of the patient. An example of this is given in another paper.¹¹ Even in normal people there is a considerable fluctuation in red cell count.¹²

Cell volume, cell count or hæmoglobin content as the basis of correction.—Gram employed cell volume¹ and later hæmoglobin content⁴ as a basis for correcting the sedimentation rate. Rourke and Ernstone² employ cell volume, and Walton³ the cell count. R. L. Haden has shown that in normal persons the ratio of cell volume and hæmoglobin content to the cell count never varies more than 10 per cent of the mean value. Hence, apart from those anæmias associated with abnormal cell volume and hæmoglobin content, it would seem that whatever objections exist to correction for cell volume are likely to apply with about equal weight to corrections based on cell count and hæmoglobin percentage. Walton's method, which requires a cell count on each blood sample, becomes very tedious where large numbers of sedimentation tests have to be carried out.

DISCUSSION

From the above, a general correction for the effects of cell volume is inadvisable. In cases of anæmia correction for cell volume *reduces* the number of results which are in good accord with clinical findings. Correction for cell volume appears to have definite value only for limited conditions, *i.e.*, for blood samples having over 105 per cent cell volume, which have a low sedimentation rate. Here correction as a rule does not seriously influence the clinical significance of the results.

The data obtained in this work agree with those of Westergren⁷ who states, "The important influence which theoretically might be expected as a result of the effect of cell volume is in clinical experience very much less." As in our experience, he finds some justification for cor-

rection in those cases having a high cell volume but relatively low sedimentation rate. In a later article, Westergren, Theorell and Widström⁸ observe that, "Most authors seem to have found that in practice the effect of anæmia in general plays no decisive, or at least only a disturbing, part." This view is also sustained by Lebel and Lottrup,⁹ out of 363 tests they found either the corrected or uncorrected rates to be satisfactory in 299 cases. Of the remaining 64 tests, in 46 cases only the uncorrected sedimentation was in keeping with the clinical features of the case, and in 18 cases only the corrected sedimentation.

To correct the sedimentation rate for the effect of cell volume adds appreciably to the time and attention which is necessary to complete the test, and cannot be justified unless the corrected sedimentation rate is definitely more accurate and reliable than the uncorrected rate. The evidence presented herewith indicates that correction for cell volume actually reduces, on the average, the clinical value of results from the sedimentation test.

SUMMARY

Correction of the sedimentation rate, whether on the bases of cell volume, cell count or hæmoglobin content, is in general inadvisable, as it introduces greater errors than it eliminates.

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MILIARY TUBERCULOSIS IN A NEWBORN INFANT

BY GEORGE M. WHITE, M.D. AND DONALD F. W. PORTER, M.D.

Saint John, N.B.

PLACENTAL transmission of tubercle is probably a very rare condition, with very few authentic cases on record. Since many clinicians still dispute the possibility of such a mode of infection it has been decided to place the following case on record.

CASE REPORT

Maternal record.—Mrs. M.B., a primigravida, aged 32 years, first reported for examination on July 23, 1936. Her history of previous illnesses was that of ordinary childhood diseases, including rheumatic fever, with good recoveries. There was a definite family history of tuberculosis. Her mother died of pulmonary tuberculosis at the age of fifty years and one sister at the age of twenty-three years of the same condition. Patient was exposed to infection from both these relatives. Her menses began at sixteen years of age, and occurred regularly every four weeks, lasting five days with a moderate flow. She had severe dysmenorrhœa. Patient was married at the age of twenty-four years and this was her first pregnancy. Last menstrual period began on April 27, 1936, and she was quite well up to the time of examination except for a long-standing constipation. The general examination was quite normal. Teeth and throat healthy. Thyroid gland was not palpable, and there was no general enlargement of the lymphatic glands. Her lungs were carefully examined and no clinical evidence of any disease of the lung tissue found. Her circulatory, gastro-intestinal, and urinary systems were all found to be normal. Pelvic measurements were normal and pelvic examination showed a uterus which corresponded in size to the period of amenorrhœa. From July 23, 1936, until February, 11, 1937, she was examined regularly when temperature, pulse, respirations, blood pressure, urine and weight gains were normal at all times. The blood Wassermann was negative. Iron medication was given during pregnancy and at the time of labour her red blood cells were 4,500,000 and her hgb. 95 per cent of 13.78 g.

Labour began February 12, 1937, and after eight hours' labour she was delivered, spontaneously, of a female child from a right occipito-anterior position. Placenta was normal to usual macroscopic examination and no microscopic was done as this case was considered normal at the time of delivery. During the lying-in period in hospital, mother's temperature and pulse were normal. Her milk supply failed and she was discharged from the hospital on the twelfth day with pelvic organs well involuted for that period, and her general condition good.

Baby record.—The baby was admitted to the nursery with temperature 96.8°, weight 7 lbs. 10 oz., length 21 inches. Routine admission bath was administered and ammoniated mercury ointment applied to entire body. Eyes were irrigated with normal saline. Alcohol dressing was applied to cord. Twenty-four hours after admission, the temperature was elevated to 103°; eight hours later it had dropped to 101°, and within twenty-four hours was normal. During this first two days the infant received lactose solution at four-hour intervals by mouth, and after the first twenty-four hours a dilute cow's milk formula was started. The only abnormal feature noticed in the first forty-eight hours of life, other than the fever, was an abnormal dryness of the skin. A diagnosis of inanition fever was made, and the infant was given 50 c.c. of normal

saline subcutaneously in addition to extra fluid by mouth. The infant maintained its birth weight in the first four days, and in fact the weight remained between seven and eight pounds throughout life. On the fourth day the temperature gradually rose again, and from that date until death the temperature was of a septic type varying between 100 and 104°. A moderate amount of abdominal distension was noted in the first week, and was well controlled by an occasional warm water irrigation. About the third day the infant commenced breast feedings with complementary whole milk dilution formula.

By the end of the first week it was found that the baby had maintained its birth weight, and the only two abnormalities noted on physical examination were moderate dryness of skin and some transient circumoral cyanosis. The infant then, for the first time, began being drowsy and moderately irritable when handled. On the ninth day three stools in succession contained small amounts of bright blood and mucus. A tentative diagnosis of hæmorrhagic disease of the newborn with intracranial hæmorrhage was made, although it was fully realized that both these conditions are usually manifest in the first week of life. Twenty c.c. of paternal blood was given intramuscularly and two hours later lumbar puncture was done. The spinal fluid flowed readily but under no increased pressure, and the fluid was very bloody. The baby was put immediately on intracranial orders, and for the following two days the colour was better and there was only very occasional vomiting. Intramuscular whole blood was again given on the tenth and eleventh days. At this time it was first noted that inconstant crepitations were present in both lungs, and that the spleen was barely palpable; 0.10 c.c. of 1:10,000 old tuberculin was given intradermally and proved to be negative in twenty-four hours and forty-eight hours. White blood count 17,900.

The following week presented very little general change in the infant's condition. Transient cyanosis was present which was relieved with oxygen; septic temperature was maintained. Feedings were sufficiently well taken to maintain weight, and blood in small amounts was present at intervals in both stools and vomitus. Intramuscular blood was repeated at intervals, and lumbar puncture was repeated on the sixteenth day of life. The fluid flowed freely with no increased pressure, and was only slightly blood-tinged. The child received a transfusion of 50 c.c. of whole paternal blood on March 2nd and an additional 30 c.c. on March 6th. By one month of age the crepitations, which previously had been inconstant, were now heard at all times throughout both lungs; the liver and spleen were both enlarged and the infant's general condition unchanged. By this time also it had become evident that the infant was suffering from a general septicæmia with hæmorrhagic manifestations, or possibly a generalized tuberculosis. Blood culture done early in the third week of life was negative at 18, 24 and 48 hours. Bleeding time 8 minutes, clotting time 4½ minutes, and platelet count 150,000. White blood count 20,000. X-ray examination of the chest by our roentgenologist, Dr. A. S. Kirkland, during the fifth week showed, "the presence of a diffuse grayish mottling throughout both chests which has the appearance of a widely dispersed bronchopneumonia, which I am unable to differentiate from a possible tuberculosis. The spleen and liver both appear to be enlarged."

At the end of the fifth week, a second blood culture was taken, giving a positive report for *B. influenza* (this was later considered to be terminal bacteræmia).

At this time abnormal findings in the chest were still present, liver and spleen were still large, and the child's general condition showed no material change. The second chest x-ray at this time showed "the presence of broncho-pneumonia throughout the right lung and at the left base". A second intradermal injection of old tuberculin was negative in twenty-four and forty-eight hours. White blood count had dropped to 10,000 although there was no material difference in the temperature readings.

The infant developed a gradually increasing cyanosis in the final five days of life and this at times was relieved partially by oxygen. It died quietly 46 days after birth.

Autopsy was performed by Dr. R. A. H. Mackeen. "This body is that of a poorly developed, poorly nourished, white female infant. Rigor mortis is present. There is dependent lividity. Pupils are equal and measure 4 mm. There is no oedema.

Peritoneal cavity.—Contains slight excess reddish fluid. Appendix shows no special change. Mesenteric lymph nodes are enlarged and caseous. Tubercles are sprinkled upon the serosa of the small bowel and in the omentum.

Pleural cavity.—Right and left. Slight excess straw-coloured fluid. Both lungs are partially consolidated and the serosal surface is peppered with miliary tubercles, some of which have fused and measure up to 7 mm. in diameter. Cut surface of both lungs shows them to be the site of miliary tuberculous broncho-pneumonia. The hilus glands are enlarged on both sides and are caseous.

Pericardial cavity.—No excess fluid. Heart appears normal in size and shape. There are no valvular defects.

Spleen.—Much enlarged. Measures 10 by 6 by 4 cm. Surface is studded with yellow areas of necrosis which measure up to 1 cm. in diameter. On section substance is plum-coloured, fairly firm, but is studded with tubercle follicles up to 1 cm. in diameter. Shows some caseation.

Gastro-intestinal.—There is beginning tuberculous ileitis and colitis present, with a few shallow ulcerations noted.

Pancreas.—No special change.

Liver.—Slightly enlarged, studded on the surface and internally with miliary tubercles.

Kidney.—Right and left. Appear normal in size. Both beneath the capsule and in the substance there is miliary tubercle formation. Calyces and ureters appear normal. Adrenals, bladder and genital organs, no gross change.

Aorta.—Smooth and elastic.

Head.—Calvarium, normal thickness. Dura appears smooth. Meninges are congested. Brain substance shows no gross lesions.

Middle ears.—Show no gross change.

Pathological diagnosis.—Miliary tuberculosis.

Microscopic examination.—Lung, tubercles with necrosis and tuberculous pneumonia. Kidney, numerous tubercles with necrosis. Spleen, tubercles with necrosis. Glands, almost complete destruction of glands. Brain, no tubercles found, congestion."

COMMENT

This case calls for a consideration of one of two modes of infection of the infant: (1) prenatal and (2) postnatal.

The possibility of a postnatal infection was investigated by examining all those who were in intimate contact with the infant in the first week of life. This included chest x-ray investigation of the two attending physicians, the intern and the nurses on the case. All of these were considered non-tuberculous from a clinical

and x-ray point of view. On April 10, 1937, the mother and father were both examined and x-rayed by Dr. R. J. Collins, Medical Superintendent of the Saint John Tuberculosis Hospital. He reported: "Examination on Mr. H.B. did not show any evidence of either past or present tuberculosis."

"In Mrs. H.B., there were evident at both apices two calcified areas with no surrounding reaction, which would seem to indicate that she had had a childhood tuberculosis." We are therefore down to the point where it is really impossible to incriminate either the father or the mother in the tuberculosis of the child, from the standpoint of sputum-borne infection. It is hard to conceive of the mother having had tubercle bacilli in her sputum when she had neither sputum nor an open lesion. Furthermore, all nurses, interns and physicians in contact with this infant carried out the mask technique which is routine in this nursery.

A further report on Mrs. B. by Dr. Collins on May 18, 1937, reads:

"The extra pulmonary structures show nothing of note. *Right lung.*—There is definite calcification area in the extreme right apex and slight clouding. The remainder of the lung field is clear. *Left lung.*—Also shows calcification in the root and several small calcified areas in the apex and first interspace. There does not appear to be any recent localization in this film, but there is definite evidence of latent tuberculosis."

The pelvis also was reexamined on May 18, 1937, and found to be free of any evidence of tuberculosis. Since that time the mother has regained her usual health and has been able to carry on with her housework. She has had no evidence of any active disease in her chest.

In considering the possibility of prenatal infection, one must presuppose blood stream infection in the mother. If this had occurred at any time up to the seventh or eighth month it would have resulted in a dead or marasmic infant. Blood stream infection occurring in the last two weeks of intrauterine life might explain the whole picture. Tuberculous involvement of the placenta, causing systemic disease in the infant, either in the last few days of prenatal life or possibly early in labour, would seem to be the more probable explanation in our opinion.

As regards the time of onset of symptoms in this infant, we feel these became manifest not later than the fourth day of postnatal life. With the subsequent course of events, one might even question the diagnosis of "inanition fever" in the first two days of life, as the usual sharp loss of weight was not present in this case.

THE DEPARTMENT'S RESPONSIBILITY FOR FOOD PROTECTION*

By R. E. WODEHOUSE, O.B.E., D.P.A., M.D.

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Ottawa*

CONTAMINATED FOODS.—Infected food is more often an epidemiological problem than those usually included in the consideration of the administration of the Food and Drugs Act. However, it should be mentioned that the Federal Department maintains a Division of Epidemiology and would gladly lend its aid to any Provincial Department desiring it. The Federal Department also has an interest in infected food supplies in the following ways. It certifies to the sanitary safety of all shipments of shellfish for export to the United States of America. The same service is carried out by the United States Public Health Service for shellfish intended for Canadian consumption, harvested in the United States of America. Further, the Federal Department of Pensions and National Health, through its hygienic laboratory staff and its division of sanitary engineering, aids the Federal Department of Fisheries by reporting upon shellfish areas under its control, providing products for consumption in Canada. The sanitary engineering division also supervises all water supplies for drinking or culinary purposes on all common carriers, more especially in international service. It carries out sanitary supervision, which includes water supplies, of all national parks and federal public works.

Expanding activities.—The Federal Department of Pensions and National Health spends annually for the control of food and drugs, including shellfish work and the other items mentioned above, approximately \$150,000. It maintains 27 food inspectors (London has a district office under Mr. E. B. Thurlow); 6 laboratories employing 61 workers; 5 sanitary engineers; epidemiologist, and a staff of 3, without counting the time of executive administrative officers devoted to these activities. They never seem to get caught up with the pressing demands for their services. The function of the department is constantly changing

in so far as the requirements of the Food and Drugs Act are concerned. The control of the merchandising of articles of food, stated to contain vitamins, is one of our newer enterprises, and required additional laboratories and staff, as well as increased supplies of test animals. The detection of the deadly poison which sometimes develops in July and August in certain mussels is urgent, in order that counteracting agents may be devised and recommended and tests established to show the absence or presence of the poison in these shellfish. Metallic poisons resulting from the processing of foods, or accumulated from the preservatives used or from the containers in which foods are stored, have to be eliminated. Constant vigilance must be maintained to prevent attempts to use synthetic and other substitutes for the colouring agents, preservatives and solvents, approved for prescribed uses in the Food and Drugs Act of Canada. This Act is probably the most effective legislation of its kind on the statute books of any country today. It is held to be administered consistently, always with the interests of the consumers and honest merchandising paramount.

WHAT IS FOOD?

The Revised Statutes of Canada—1927, Chap. 76, Section 2 (d)—an Act respecting Food and Drugs—state:

“Food includes every article used for food or drink by man, and every ingredient intended for mixing with the food or drink of man for any purpose whatever.”

It will be agreed that this is an all-inclusive definition. You would expect it to include liquid milk, but the standard for this has now been omitted from the regulations and passed to the control of the Provincial Health Acts. The Meat and Canned Food Act also assumes some details of control in this field and thus overlapping is avoided. However, as the Food and Drugs Act is operating to control the whole federal food field, it has been expressed in legal opinion that it supersedes, if ever necessary, any other Statute dealing with only

* Paper given before the Annual Convention of the Dairymen's Association of Western Ontario, January 12, 1938, at London, Ont.

a part of the field, and of course supersedes, if confronted with a difficulty, all Provincial Acts and Regulations. This conflict, in so far as I know, has never developed in actual practice.

Under the regulations authorized by the Food and Drugs Act, prescribed standards of quality for, and fixed limits of variabilities permissible in, articles of food are set up, if not otherwise prescribed by this Act or the Meat and Canned Foods Act.

The Food and Drugs Act definitely stipulates that labels will be attached to articles of food, and delineates for the protection of the consumer and the producer the freedom with which these may be worded. The food products must be designated by their common names in one or other or both of the official languages.

The term "Blend" shall be applied only to a combination of similar substances. A combination, for instance, of coffee and chicory is not a blend—it is a mixture or compound and must be labelled as such. The ingredient in a compound making up 51 per cent by weight is the ingredient governing the choice of marketing name.

A distinctive name shall give no false indication of origin, character, or place of manufacture, nor lead the purchaser to suppose that it is any other food product. For instance, thanks to this stipulation, Scotch Whiskey, as sold in Canada, must be distilled in Scotland.

MISBRANDING

The Food and Drugs Act forbids imitation or substitution by one merchandiser of the labels or branding of another, nor must the labels resemble each other in a manner likely to deceive. A food must not be coloured, coated, powdered or polished, to conceal damage to the product or to make it appear better than it is.

It must not be marketed in a package (underfilled) of a size out of proportion to the volume of the contents.

The use of the words "pure" or "genuine" or words equivalent to these terms is not permitted in the labelling of compounds, mixtures or imitations.

Foods may be seized for misbranding by inspectors appointed under the Food and Drugs Act. Vendors, upon summary conviction, may be fined from \$25 to \$100, or imprisoned for

3 months, or receive both fine and imprisonment for the first offence: or \$50 to \$200, or six months' imprisonment, for the second and subsequent convictions.

ADULTERATION

You will be surprised to learn that honey offered for sale that has been produced by bees fed with sugar, except for the purpose of being consumed by them as food, or with glucose or any sweet substance other than such as bees gather from natural sources, with the intent that the same shall be used by the bees in the making of honey, shall be deemed wilful adulteration of honey within the meaning of this Act.

Adulteration may consist of abstracting in whole or in part some valuable constituent of the article of food, (for example, in sterilized milk, extracting butter-fat and leaving less than 3.25 per cent).

It is forbidden to add inferior or cheaper substances as a substitute wholly or in part for the article. In the last few years we seized and destroyed over 6 tons of white pepper, some of it containing a filler of rice flour. The food must not be, or manufactured from, diseased, putrid or rotten animal or vegetable substance, nor obtained from a diseased animal or from an animal fed upon unwholesome food.

It has taken the department several years to break down the practice of offering spirit vinegar as malt vinegar, simply by changing the colour with the addition of caramel solution or burned sugar. Recently we have seized for destruction in this province and in the west 1,598 gallons. Another infraction is offering for pickling recipes or other purposes "Acide Vinaigre", a diluted acetic acid.

Carloads of nuts and figs have been turned back at our customs ports on account of having, upon examination of samples in our laboratories, too high a proportion of spoiled, mouldy, or shrivelled products. The change in recent years in these products offered in Canada must be evident to all housewives. Certainly, the trade is conscious of the improvement.

In all our laboratories last year 20,000 samples, deemed suspicious by our field inspectors, were examined. You will be surprised to know that more than half of the samples examined came from importations sampled in the customs warehouses. Of 10,000 more im-

portant foods tested from suspected sources nearly 25 per cent were classed as adulterated or misbranded. They included everything from macaroni and spaghetti, which are classified—"Alimentary Pastes", which brings them first in the alphabet, to "Acide Vinaigre" also starting with "A" but classified under "Vinegar" in the last of the alphabetically arranged list.

FOOD STANDARDS

In order to arrive at what is adulterated and what is not one must have set standards for guidance. These are contained in the regulations under the Act. They cover seventeen categories, proceeding from baking powder to waters (bottled waters). Beverages include fruit drinks, fresh, sweet and fermented, malt liquors and malt beverages, and spirituous liquors. Also included in the groupings are flavouring extracts, metallic impurities, preservatives, and milk products. Under milk products eighteen standards are listed—among other things, setting forth the butter-fat content of sterilized milk at 3.25 per cent, defining condensed milk, evaporated milk, sub-standard concentrated milk, skimmed milk, condensed skimmed milk, defining milk fat or butter fat, butter itself, whey butter, cheese made from curd obtained from milk, cheese made from and by the use of skimmed milk, ice cream, whey, kumyss, milk powder, skimmed milk powder, malted milk, canned homogenized milk, and chocolate-flavoured dairy drink.

Merchandising of foods is, considered as a whole, on a very high plane. It is one of the most scientifically controlled lines of production, and by this I mean the producers and their group associations provide themselves with well assembled laboratories, possessing as capable personnel as are obtainable, and any technical equipment the staff request. This is as it should be. Competition demands it and thus the consuming public benefits. Newcomers through their lack of appreciation of the requirements are mostly responsible for attempts to infringe on the stipulations of the statutes and its regulations, as well as upon the good name usually enjoyed by the legitimate merchandising group. These attempts are mostly due to greed for profit; over-keenness for volume of trade causes them to chisel quality in order to reduce price. They are ignorant or careless of the morale operating in the different

branches of food merchandising. They also attempt these offences through lack of respect for law enforcement agencies and their equipment. Our staff always try to be reasonable, but sometimes this group, who are so persistent in their marginal practices, prove rather trying. An odd case occurs of utter disregard for human life and health, in the pursuit of gain. We also have the less serious attempts to gain advantage of the public. The Food and Drugs Act was framed to consider the economic as well as the physical welfare of the consumer.

NUTRITION

Under this heading the writer presided at an afternoon session of the English-Speaking Conference on Child Hygiene in the other London last summer. It was stated by the chairman there were at least four phases of the subject of the symposium which suggested themselves, namely, (1) the technical or laboratory field; (2) the clinical estimation in individuals of their nutrition; (3) the agitation for nationally larger consumption of certain foods, and, lastly, the social, economic and controversial phases of whether the wages paid would buy a sustaining diet. It was desired that any speakers would discuss only the first two, as they were the subjects of the two program contributions. My conception of what the Canadian National Council on Nutrition will be asked to consider at Easter will easily fall under the two first headings.

The most extensive studies of food consumption in Canada so far have been made on dairy products. This is likely due to dairy associations interesting themselves and others. Studies have been made of the budgeting for foods in typical families. Also other households have cooperated to permit expert supervision in their homes of the normal buying and preparation and serving of foods and estimates to be made of the quantities and varieties used daily and weekly by each individual member of the family, so that costs for age groups could be calculated. These fundamental factors are felt to be essential, and, once established, will provide a proper basis for national appraisal. Possibly it may develop that in Canada the most difficult time to maintain the essentials of diet is in the winter. We are convinced of this in our laboratory animals. Fatal infections in our breeding stock are materially decreased

by assuring as good a supply of vitamin C-containing foods as we naturally have in summer. Oranges are not the only source of supply of vitamin C or ascorbic acid. I am informed that turnip juice, which should be cheap enough to secure, does the trick. It is also said that synthetic ascorbic acid lacks something essential found in the fruit and vegetable sources of vitamin C. Some studies in Ontario have shown that the same vegetables grown in different localities possess different percentages of essential salts.

It is just such things as those referred to above that we hope to have studied concurrently by different groups in various parts of

Canada, under exactly the same methods, in order that the findings will be such as to lend themselves to useful comparison.

Possibly our increased infections in winter-time are mostly due to faulty diet and, in a very small way, to our over-heated houses and close, too intimate and continuous, contact. If we can point out the proper foods to maintain our resistance to disease, obtainable at a cost within the family budgets of all of us, and teach our people helpful things about cooking and serving these, I am sure you will all agree the government will have been well advised in establishing the Canadian National Council on Nutrition.

Case Reports

ACUTE RHEUMATIC FEVER WITH UNUSUAL COMPLICATIONS

By H. S. GOOD AND B. KANEE,

Weyburn, Sask.

Mr. J.S.D., white, aged 54, and of Swedish descent. His previous illnesses were a right inguinal herniotomy in 1926; ischio-rectal abscess in 1935. His present illness was preceded by an attack of "flu" of about three weeks' duration, and on March 14, 1937, he was admitted to the Weyburn General Hospital, complaining of sore throat, pain in his left shoulder region, precordial pain and dyspnoea. His temperature at that time was 101°; pulse 118; respiration 22; blood pressure 120/80; urine negative. Examination revealed redness and swelling of his left shoulder and a systolic murmur at the apex. He was put on heavy doses of salicylates, light diet, and his left shoulder was wrapped in flannels following the application of methyl salicylate and radiant heat applied. An ice cap was applied to the precordium. Examination the following day revealed a fibrillating heart, at a rate of about 120 a minute; and a definite pericardial friction rub at the apex. The patient was having considerable pain and dyspnoea. He was then rapidly digitalized.

With a very good response to both the digitalis and salicylates his temperature and pulse gradually returned to normal. However, he subsequently developed pain and swelling in his right thumb, right hip, and left knee, at about three-day intervals respectively, which in turn responded to the afore-mentioned line of treatment.

On March 22, 1937, the patient began to complain of nausea, which persisted despite the discontinuance of the digitalis and salicylates. His blood pressure at this time was 120/80; urine negative. His nausea continued, and on the 30th he vomited, following which he had a gastric lavage which afforded him considerable relief. His nausea and vomiting however still persisted, and on April 3rd he complained of a severe headache. Examination then showed a blood pressure of 190/100, and there was a diminished urinary output; the urine contained albumin, red blood cells, hyaline and granular casts; the specific gravity was 1.010 (morning specimen). His tongue was brown and dry and his breath heavy.

Thus we now had to deal with a case of acute Bright's disease, which problem greatly overshadowed his original illness on admittance and the following regimen was started: (1) hot packs twice a day; (2)

500 c.c. of 5 per cent dextrose in saline intravenously once or twice a day as deemed necessary; (3) ½ oz. of magnesium sulphate, two doses at hourly intervals daily when tolerated; (4) colonic irrigation twice a day; (5) luminal, gr. ½, as required.

On April 6th his heart again began to fibrillate, but soon settled down with rapid digitalization. Twitching of his left arm was observed at this time. On April 8th he developed a phlebitis of the left great saphenous vein, and was observed to be becoming drowsier. His kidney picture remained stationary; i.e., diminished output, low fixed specific gravity, casts and blood, and he was gradually sinking into a uræmic state. For the phlebitis we immobilized and elevated the affected leg, and applied heat plus the use of a cradle. Linseed poultices now replaced the hot packs. On April 9th he developed a phlebitis of the right popliteal vein, which soon spread up and down the right leg; also at this time œdema of the sacral region became quite marked and he was finding great difficulty in breathing. His temperature was 98.1°; respirations 24; and pulse 100. Chest examination at this time showed considerable dullness of the left lung, extending up to the third interspace and displacing the heart to the right. The chest was aspirated and 1,500 c.c. of a clear straw-coloured fluid were withdrawn, the specific gravity of which was 1.012. This afforded him considerable relief, as was also evidenced by his pulse going down to 88.

On April 11th we aspirated 900 c.c., and on April 12th again aspirated 740 c.c. Following this he did not develop any further sieges of hydrothorax, but there was considerable fluid in his abdomen, the pressure of which resulted in urinary retention, necessitating regular catheterizing. The patient gradually became weaker and more drowsy from day to day, and muscular twitchings now spread, to involve both arms. He was still nauseated, with spells of emesis, his tongue remained dry and brown, and he had a profound thirst.

On April 16th the progressiveness of his condition was evidenced by the marked twitchings which now involved both arms, face, and body. His mind was greatly confused, but he still had lucid intervals. During the next week or two he was also troubled with pains and swelling of his joints which only lasted a day at a time, and the remarkable feature about this case was the normal temperature dating from April 4th to 24th. On April 24th he developed a left parotitis associated with considerable pain. His temperature gradually mounted, his twitchings became violent, his mind more confused, and his chest and lungs gradually filled up with fluid. And over a period of six hours he gradually

lapsed into coma, became cyanosed, his breathing became laboured, and, despite a venesection, oxygen, and coramine, he continued to fail rapidly, and finally drowned in his own secretions, a victim of uræmic poisoning.

SIMULTANEOUS BILATERAL SPONTANEOUS PNEUMOTHORAX COMPLICATING BRONCHIAL ASTHMA

By G. S. JEFFREY, M.B. AND
D. C. MARLATT, M.D.

Fort William Sanatorium

In the September issue of the *American Review of Tuberculosis*, 1936, Glickman and Schlomovitz reviewed the 82 cases of simultaneous bilateral pneumothorax that had been reported in the literature up to that date. Of this number 48 per cent were due to pulmonary tuberculosis, 21 per cent were idiopathic, and 12 per cent were due to emphysema.

The following case, a boy of 17, was referred to the Fort William Sanatorium in July, 1937, by Dr. W. J. Henry, of Jellicoe. There was no history of contact with tuberculosis. The mother was a chronic asthmatic. For the past four years he had been subject to attacks of bronchitis each spring, lasting about two weeks but unaccompanied by asthmatic symptoms. He had suffered repeated mild attacks of tonsillitis for several years. Fourteen months previously he had weighed his maximum, 114 pounds. Early in the previous winter he had developed a cold with cough and mucoid expectoration which persisted. Shortly after he began to have attacks of asthma, and for about two months previous to admission to Sanatorium, July 21, 1937, his dyspnoea had been practically continuous. On a number of occasions the sputum had shown slight streaks of blood. About June 10, 1937, he developed pain in the left chest lasting for several days, and subsequently transient pain in the right chest. He had only recently received medical attention.

On admission he weighed 74 pounds. He was obviously dyspnoeic at rest, with cyanosis of the nails and extraordinary development of the sternomastoid and abdominal muscles from heavy breathing. The chest showed the pigeon type of deformity with retraction over the lower ribs bilaterally. The breath sounds were absent at the apices and heard only feebly over the balance of the chest. Scattered rhonchi were heard throughout both sides of the chest. Following hypodermic injection of 5 minims of adrenalin all rhonchi rapidly cleared and his dyspnoea was obviously improved. Several carious and septic-looking molar teeth were present. His tonsils were large and obviously unhealthy. X-ray of the chest showed the presence of a bilateral pneumothorax with a uniform collapse of both lungs, to the extent of about 60 per cent. A few thread-like adhesions were present laterally in the midlung area and at the left apex. The linear shadows appeared to be generally increased. There was no evidence of parenchymatous disease. The red cell sedimentation rate was only 3 per cent in one hour on admission. Sputum tests were negative for tubercle bacilli on both direct smear and culture. Intracutaneous tuberculin test showed only a minimal reaction.

The boy was put on a mixture with potassium iodide and ephedrine with marked relief of his dyspnoea and progressive improvement in his general health. Repeated fluoroscopic examinations showed that both lungs

were slowly re-expanding, and no attempt was made to hasten this process by aspiration of air. X-ray, September 1, 1937, showed that both lungs were completely re-expanded, and confirmed the previous finding that there was no evidence of pulmonary tuberculosis. He showed a temperature of 99 to 99.4° on a few occasions only; for the most part during the few days following the extraction of his diseased molars. On September 2, 1937, having gained 14 pounds in weight, he was transferred to the McKellar General Hospital, where his tonsils were removed uneventfully under general anaesthesia. He was shortly after discharged to his home very much improved in general health, but still showing a slight tendency to asthma on damp days.

It would appear that the etiological factor in the development of this boy's bilateral pneumothorax was the rupture of small emphysematous bullæ on the surface of the lung.

CHRONIC ACNE VULGARIS (INDURATA) IN MIDDLE-AGED WOMEN

By A. HOWARD PIRIE

Montreal

Acne which persists for years in a woman past thirty-five can have a very depressing effect on her nature. She is so conscious of her unsightly appearance that she shuns society and develops an inferiority complex. As time goes on and no improvement appears she loses hope of ever being presentable in public, and thoughts of suicide may even be entertained.

The following case illustrates the change of character brought about by the cure of acne of thirteen years' duration in a woman of 38.

Miss B. had tried everything to rid her face of acne indurata. When first seen in 1936 her face was deeply pitted by scars of healed acne and was lumpy all over with indurated red swellings which gradually came to a head after a month and took from one to two months to disappear, leaving bad scars behind. In order to keep her position in business she spent an hour each morning filling up the scars and levelling off the surface with "Covermark", a special facial preparation, so that she could powder her face and look presentable. In spite of trying many remedies her face grew worse, and she was despondent to such a degree that it was spoiling her whole nature. Then she began to notice that at menstrual periods her face was always much worse, and she reasoned that if her menstruation could be stopped the disease might be checked. So she consulted a gynaecologist and he in consultation with another gynaecologist advised her to try the effect of sterilization by x-rays. She welcomed the advice and the sterilization was carried out by x-rays. The acne disappeared at once, but later on a few spots appeared which marred the result. A course of x-ray treatment was then given to her face and a perfect cure was obtained. A year later she remained cured, and as a result of this cure the change in her outlook was great. She has regained her normal cheerfulness and is again enjoying the pleasures of society, the depressing thoughts of suicide have vanished, and she has sufficient self-confidence in her appearance to have taken a trip abroad.

A sister of this patient also has had acne for years. She wished to have the same treatment

of sterilization, but on account of probable marriage I suggested to reverse the order and gave a complete series of x-rays to her face first. This has not cured the acne, and she is now about to have sterilization, hoping that she will recover in the same way as her sister.

It is justifiable to produce sterilization in a

woman of forty who has suffered from acne for years, and thereby give her the chance to feel that life is worth living again. One does not see acne of any importance in women after the climacteric period, so it seems reasonable to infer that sterilization will stop the process and should be resorted to in certain cases.

Therapeutics and Pharmacology

THE TREATMENT OF CONSTIPATION

By H. GODFREY BIRD

Gananoque

The treatment of this very common complaint is greatly neglected by the physician, a fact borne out by the multitude of newspaper, magazine and radio advertisements of proprietary preparations for its relief. The majority of persons who are really constipated do not suffer from delay in the passage of faeces through the intestines but from inefficient defaecation. It is not wise to give purgatives to every patient complaining of constipation, as they are either absolutely useless or produce large fluid stools, with the waste of fluid and nutritive material. An excessive amount of bran and other coarse food in the diet may cause considerable damage to the mucous membrane of the pelvic colon, where the hard particles remain in contact with the mucosa for a considerable time.

In all cases of constipation organic disease must be ruled out. In the nervous patient who fears cancer or obstruction of the bowels the mental effect of a thorough x-ray and sigmoidoscopic examination is of the greatest value. In all patients suffering from constipation a few minutes devoted to an explanation of normal bowel action will be well repaid. The patient should be impressed with the importance of going to the closet shortly after breakfast each morning regularly. It is not necessary that he have a desire to go. The desire must be reacquired by patient effort and training. The rectum is normally always empty except immediately before defaecation. Food taken into the empty stomach stimulates the intestines and some of the faeces accumulated in the pelvic colon is forced into the rectum, initiating the desire to defaecate. Neglecting to empty the rectum, allowing it to become tolerant of the presence of the faecal mass, is the most frequent cause of constipation.

To increase peristalsis, the patient should be instructed to take a cold bath and drink two glassfuls of cold water on rising. Smoking after breakfast has the same effect. If the faeces are dry and hard the patient should use a stool for his feet to bring his knees to the squatting position. He should be encouraged to make

strong expulsive efforts and be assured that he cannot harm himself in doing so. He should be made to understand that complete evacuation of the bowels takes place in two parts. First the rectum is emptied, then the descending colon. An interval of time elapses between the evacuations, and the patient must not hurry. Here the morning newspaper plays a useful part. The lavatory should be warm and as pleasant as possible.

The patient must not be discouraged if his bowels do not move the first few mornings. He must be assured that occasional failure to open his bowels is not dangerous. If his bowels move at all without artificial aid he has scored a victory, and he should feel encouraged. Too careful scrutiny of the size of his movements will tend to make him impatient of progress, and this should be discouraged.

During the day the patient should take all the exercise possible. Walking, out of doors, up and down hill, is the very best form of exercise. This should be carried to the point of mild fatigue. The casual walking around two or three city blocks is not to be considered satisfactory exercise in the average case. If at any time during the day the patient has desire to defaecate he should obey the call at once. He should be impressed with the fact that he is re-educating a reflex that has been dulled by neglect.

If, after two days, a bowel movement has not occurred the patient may take a low enema of cool water to empty the rectum. Rarely will he require to take an enema more than two or three times before regularity is established.

In regard to diet and eating habits. The patient should, of course, get up for breakfast. The act of getting up and dressing stimulates the gastro-colic reflex. Food should be well chewed and sufficient food should be taken. In many cases of neurasthenia in thin patients an increase in the diet, combined with mental and physical rest, cures the constipation, as well as the nervous condition. Most patients who come to the physician complaining of constipation have already tried eating bran, raw fruits and vegetables, and whole wheat bread with indifferent success. Combined with the other measures outlined, however, such foods are definitely useful in some cases, causing the faeces to pass

to the rectum more quickly, so that they are softer and more bulky, and consequently require less force for their expulsion. Those suffering from hæmorrhoids should, however, avoid the coarse diet, as the residue is most irritating to the mucous membrane in these conditions.

PAROXYSMAL TACHYCARDIA

BY W. FORD CONNELL

Kingston, Ont.

The term, "paroxysmal tachycardia" implies a condition in which the heart *suddenly* becomes rapid, and, after a variable period of time—seconds, hours or days—just as suddenly reverts to normal action. Such attacks of rapid beating of the heart are always due to the inception of a completely abnormal cardiac rhythm. For example, we may find both auricular fibrillation and auricular flutter occurring in paroxysmal fashion during the course of organic heart disease. The term "paroxysmal tachycardia" is not applied to such bouts, but is reserved for that disorder of cardiac rhythm which consists essentially in a rapid series of premature contractions, arising from some abnormal focus in the auricle, or more rarely in the nodal tissues or ventricle, dominating and maintaining a regular rhythm of 150 to 250 beats per minute.

The auricular variety of paroxysmal tachycardia is quite common. It is usually seen in persons with otherwise healthy hearts, and is hence to be regarded as an annoying but benign functional disorder of rhythm about which the patient should be thoroughly reassured. The nodal type is rare, equally benign, and can only be differentiated from the auricular variety by electrocardiography. The ventricular type is also rare but occurs invariably associated with serious heart disease—often following coronary thrombosis. In such circumstances the attacks may render the clinical picture still more grave and demand urgent treatment.

Paroxysmal auricular tachycardia is found in healthy adults of all ages; heart disease, if present, is coincidental. The paroxysms commence with all the abruptness of a premature contraction. Their duration may be a few beats or they may go on for as long as six days. Attacks lasting a few minutes are much the commonest. Absolute constancy of rate is a pathognomonic feature of the attack, neither drugs nor exercise producing any change. The cessation of the

attack is just as rapid and unexpected as its commencement.

Most persons experience considerable discomfort during a paroxysm. They complain of rapid palpitation or fluttering in the chest, with pounding of the vessels, especially in the neck. If nervous or hypersensitive they may become pale and sweat, and complain of præcordial ache, or even sharp stabs of left submammary pain, but such symptoms are of nervous origin and not of serious import. In persons with some complicating organic heart disease true angina pectoris may rarely be brought on by a paroxysm, or the symptoms and signs of congestive failure may be brought on in such persons (particularly if the attack be prolonged), only to clear up rapidly with the cessation of the attack.

Individual patients may know of some unusual posture or movement which will control their paroxysms. Most attacks subside more quickly with the patient at rest. There is no known treatment which will certainly stop an attack. Usually none is necessary, apart from copious doses of reassurance together with small doses of bromide or phenobarbital to quiet apprehension.

Many and various procedures, most of which aim at reflexly stimulating the vagus, are at times successful in aborting an attack. Simple apnoea (prolonged holding of the breath) pressure over the carotid bulge at the root of the neck, first on the right, then on the left side, firm digital pressure (firm enough to be painful) over each eyeball in turn, the drinking of ice water, the induction of vomiting—these are a few of the measures which can be attempted.

Of drugs used to stop an attack acetyl-beta-methyl choline, an extremely powerful vagus stimulant, is the most successful. It may be given subcutaneously in doses of 20 to 50 mg. without unpleasant effect. Or quinidine sulphate may be given by mouth, 5 grains every four hours, for not more than ten doses. If the need appear urgent quinidine may be given slowly, intravenously, 3 grains, or digoxin, 1 milligram, or some other digitalis preparation for intravenous use may be tried.

When attacks are particularly frequent and troublesome it is worth while to use continuous medication for a few months. Here again, quinidine sulphate is of value, 5 to 15 grains daily. Digitalis is also of use in this connection, but, for success, the patient must be fully digitalized, usually by the administration of some 24 to 28 grains of digitalis leaf over several days, digitalization thereafter being maintained with from $1\frac{1}{2}$ to 3 grains of leaf daily.

Ventricular paroxysmal tachycardia, while only positively recognizable on electrocardio-

graphy, may usually be distinguished clinically from the more benign auricular and nodal varieties by some slight irregularity in rate from minute to minute—as much as 6 or 8 beats' change being noted. Also, there is an occasional variation in the force of the beats, detectable by auscultation. Paroxysms are usually short, but often rapidly recurrent, and of course are serious because of the grave condition of the heart muscle which commonly induces them. Their presence calls for the administration of fairly large doses of quinidine, say 5 grains every four hours for ten doses, as advised above,

with a continuation of the drug in lessened dose thereafter, to prevent recurrence of the paroxysm. It is of interest that none of the vagus-stimulating physical procedures, nor any drug other than quinidine, appears to have the slightest beneficial effect.

In conclusion, it should be emphasized only a small minority of the cases commonly seen require any treatment whatsoever. Since, however, this is a very alarming syndrome, when experienced by an uninformed patient, the importance of early correct diagnosis and careful explanation is obvious.

Editorial

THE HALIFAX CONVENTION

WE have had our annual meeting in Halifax, and with its passing another carefully shaped stone has been built into the history of our Association. Of the various aspects of these conventions none are more valuable than the professional interchange and the outpouring of warm hospitality, forming as they do the veriest elements of our life. They are the maturing of a year's labour of organization as well as an occasion for the reinvigoration of our friendships.

In these essentials Halifax played its full and expected part. Nor was that element lacking which has always distinguished our meetings in Halifax, namely, unusual historical significance. It was here that our Association in 1921 set forth courageously in search of health and strength. This year we saw the reward of that courage not only in the financial stability of our Association (and the contrast between the then of our debts and the now of our surplus is striking enough), but also in the closer cooperation of the provincial societies in their almost complete affiliation with the parent body. The significance of this development is plain on even the least consideration, but this meeting served to bring it out in sharp relief as a culmination of steady labour and wise guidance.

The details of the convention were well arranged. There is great virtue in the centralization of all the sessions under one roof. The larger centres would do well to

strive towards this end rather than split up the meetings into numerous groups at hospitals.

We missed the activities of the Section on Historical Medicine. It had a rich opportunity in such a setting as Halifax. But Dr. MacKenzie provided us with a historical treat at his luncheon to the Council in the talk on the racial origins of Nova Scotia by Dr. J. S. Martell, Assistant Provincial Archivist. Dr. Martell spoke with the authority of a well trained historian with a well furnished mind. To this he added the quality of being able to present his material with a clarity and attractiveness that produced keen mental delight.

Another striking address was that by Prof. A. Stanley Walker, President of King's University, on liberty of thought in the learned professions. We hope to publish both these addresses later on.

Mention must also be made of the fourth Osler Oration delivered by Sir Humphry Rolleston. Sir Humphry gave us of his best, adding several reminiscences of Osler to the many already recorded. The Oration will, of course, appear in our *Journal*.

The efforts of the program committee were fully rewarded by the smooth succession of section meetings and general sessions. A word must also be said for the excellently arranged and instructive exhibits. All in all, we were given a warm welcome to a soundly planned and well executed annual meeting.

H.E.M.

VITAMINS AND CANCER

IN view of the widespread interest in the vitamins and the realization of the fact that they play a controlling rôle in certain important metabolic processes it is not surprising that some should have been moved to investigate the part, if any, which they take in the initiation and development of cancer. As a result of painstaking study and therapeutic tests we have come to know a good deal about the effects of a deficiency of vitamins in the food; we know much less, however, about the effects of an excess. In fact, a survey of the literature reveals that this latter aspect of the subject has received less attention than its importance would seem to warrant.

Suggestions as to the influence of diet on the production of cancer are being made from time to time. Recently, Dr. J. L. Moir¹ has advanced the view that the high maternal, tuberculosis and gastric cancer mortalities in north Wales may possibly be due to a low amount of vitamin A in the diets of the residents of this district. Unfortunately for this theory, as broadly stated, and so far as it pertains to cancer, other forms of cancer are more than ordinarily prevalent there. Dr. V. E. Hastings, of Auckland, in an informative letter,² from which we quote, says "Sir Robert McCarrison has told us that he did not see any cases of cancer during the seven years that he spent with the people of Hunza. The great consumption of apricots and the high vitamin A content of some of the Indian green vegetables suggest that the diet of these people may be high in vitamin A. Dr. Ernest H. Tipper, in 'The Cradle of the World and Cancer', states that among the two million people of the Bene tribe living in the palm belt of the Niger he saw no cases of cancer in twenty years' work there; he also informs us that these people use 4 oz. of red palm oil daily. The *Indian Health Bulletin* gives the vitamin A content of this oil as 44,000 international units per 100 grams, which represents the rather amazing figure of approximately 50,000 units of vitamin A from this one food only. Compare this with the daily intake of the people of the United

Kingdom, given in Sir John Boyd Orr's 'Food, Health, and Income', of 774 international units in the poorest group and 2,875 units in the wealthiest group." All this is suggestive, of course, but, at the best, only indicates a line for further research.

The most recent work on this subject, based on actual experiment, with which we are acquainted, is that of Dr. J. R. Davidson, of Winnipeg, who in a series of four communications³ reports the results of his experiments in feeding mice with diets high in vitamins, particularly in regard to length of life, general nutrition, and the control of tar-carcinoma. Diets rich in vitamin E and vitamins B₁ and B₂ tended to cause the treated animals to remain in good health longer, to develop tar-carcinoma later, and to exhibit the tumours less often. Also, when mice susceptible to the development of cancer are placed on a diet of high vitamin content, and are not treated with tar, but are allowed to breed naturally for a few generations, then if their offspring are placed on a diet low in vitamins and kept otherwise under the same conditions as mice which are susceptible to cancer, few of them seem prone to develop neoplasms. Of course, as Doctor Davidson properly points out, there may be other factors in the diet besides vitamins which may contribute to these results, and since his experiments have to do with tar-carcinoma in mice it is by no means certain that they apply with equal force to other forms of carcinoma or to the human being. His studies are worthy of attention, however, and should be followed up to determine whether his results are attributable to the action of one, more than one, or all of the presently known vitamins; also, whether these results are to be explained on the basis of improved general nutrition, or should be attributed to some specific action on what we call, probably incorrectly, "cancer cells".

Some reference here ought to be made in regard to some earlier work done on this important subject, work which, in general,

3. DAVIDSON, J. R.: An attempt to inhibit the development of tar carcinoma in mice: the effects of vitamins on the tumour threshold. *Canad. M. Ass. J.*, 1938, 38: 529. See also *idem*, *Canad. M. Ass. J.*, 1934, 31: 486; 1935, 32: 364; 1937, 37: 424.

1. MOIR, J. L.: Letter in *Brit. M. J.*, 1938, 1: 421.

2. HASTINGS, V. E.: Letter in *Brit. M. J.*, 1938, 1: 1390.

tends to the same conclusions. Such are the studies of Caspari and Ottensooser,⁴ Caspari,⁵ and von Gordon,⁶ among others.

4. CASPARI, W. AND OTTENSOOSER, F.: Ueber den Einfluss der Kost auf das Wachstum von Impfgeschwülsten, *Zeitschr. f. Krebsforsch.*, 1933, 38: 351.

5. CASPARI, W.: Ueber den Einfluss der Kost auf das Wachstum von Impfgeschwülsten, *ibid.*, 1933, 38: 361.

6. VON GORDON, L.: Vitamine und Krebs, *Zeitschr. f. Krebsforsch.*, 1933, 38: 398.

On the other hand the studies of Sumi⁷ and Görner⁸ point in an opposite direction. It is evident that more searching experiment is in order. We plan to deal with this important subject more fully in a later issue.

A.G.N.

7. SUMI, M.: *Gann*, 1930, 24: 239.

8. GÖRNER, A.: *J. Cancer Res.*, 1930, 14: 545.

THE VALUE OF ARTIFICIAL RESPIRATION

WE publish in this issue a paper on the value of prolonged artificial respiration in those who have apparently succumbed to asphyxiation of various types. The subject is not new. We feel, however, that there is an urgent need to bring it before the profession again. Those of us who heard Dr. Gordon Bates' startling address at the meeting in Halifax this year, will not readily forget the impressive nature of his carefully collected evidence. Dr. Bates showed that beyond any question of doubt many persons who were apparently dead from drowning, etc., were actually alive and capable of being resuscitated. What made us uneasy was the fact that there have been cases of this nature in which resuscitation has not been tried for a long enough period. Too often medical men have been inclined to judge the condition of the patient only by

examining his heart and respiration. It is now recognized that this is not enough. There may be complete absence of the heart or pulse beat and of respiration as elicited by ordinary physical examination and yet the patient may be alive and capable of resuscitation. There is abundant evidence to support this, both experimental and clinical. We hope, before long, to publish the results of investigations into the subject, but in the meanwhile we feel that it is necessary to bring out as clearly and forcibly as possible the necessity for much more general use of prolonged artificial respiration. No case of drowning, electric shock, or asphyxiation should be considered hopeless *unless rigor mortis has set in*.

We ask for serious consideration of this important subject.

H.E.M.

Editorial Comments

Sunlight and the Skin

A valuable article on this subject by Dr. D. E. H. Cleveland, of Vancouver,* is commended to the attention of the medical profession generally, in the hope that they will pass on the information contained therein to their clientèle, particularly the juvenile portion of it. We gather that indiscriminate and prolonged exposure to the rays of the sun is by no means an unmixed blessing. This is, indeed, what we would expect *a priori*. The worship of the sun dates from the remote past and is based on the solid principle that sunlight is the source of life and growth. In more modern times the cult of "the great out-of-doors", valuable as it is, for obvious reasons that we need not enter into here, has attained widespread proportions. At every summer resort we see numerous persons,

mostly young, attired, if you can properly use this word, in the scantiest of raiment, whose skins present various shades from a light pink to a deep coffee-colour. Many of them vie with one another in endeavouring to see which of them can attain the deepest coloration. Apparently this is a result of the reasoning which holds that if some is good more must be better. But, does this follow? We think not. Doubtless there are many who can stand this tanning process with impunity, but there are also some, the subjects of various skin affections, and some who have been using certain types of skin lotions, facial creams and perfumes, who run a risk of meeting trouble. Doctor Cleveland deals clearly with this phase of the subject. Apart from this, however, it must be stated that sunburn is a form of dermatitis. This means that the superficial capillaries of the skin are dilated, in some cases probably paralyzed, fibrous

* *Bull. Vancouver Med. Ass.*, 1938, 14: 132.

tissue is increased, and pigment is deposited. The skin in time becomes scaly, inelastic, shrunken, and, in short, senile. The young people, particularly the girls, should be informed that excessive exposure of the skin, especially of the face, lays the foundation for wrinkles later on. To go bareheaded may be a joy, but it brings its own retribution. Doctor Cleveland points out sunburn is more readily produced in proximity to bodies of water, snow or ice, and awnings and parasols give little protection. We can all recall seeing people whose faces remind us of a dried-up russet apple. There may be several causes for this unsightly state of affairs, but excessive exposure to the sun is certainly one of them.

Contrary to a widespread belief, the practice of going about bareheaded is not conducive to the growth of hair.

Some people definitely have an idiosyncrasy towards sunlight, and these should be cautious in exposing themselves to it unnecessarily. Here may be mentioned urticaria, vesiculo-bullous erythema, and leukoderma.

Of most importance is the onset of carcinoma. The senile condition of the skin produced by excessive exposure to sunlight and the formation of cutaneous keratoses are considered to be predisposing causes. The danger is real. Doctor Cleveland states that it is reported from Australia that the incidence of cancer of the skin of the face and hands is higher in the white population of that country than in any other country from which records are available. This is thought to be due, possibly, to the combined effects of dry air, strong sunlight, moderate altitude and a sub-tropical climate. Accordingly the public health authorities are advising those who are engaged in outdoor pursuits, particularly the men on up-country sheep-stations, to wear suitable protective head-covering, closed collars, sleeves to the wrist and protection for the hands.

Undoubtedly, this whole subject is deserving of more attention. A.G.N.

The Purpose of Organization of the Canadian Society for the Control of Cancer

The mortality table of Vital Statistics for Canada shows that cancer as a death-dealing agent ranks second. The number of deaths for which it is responsible is exceeded only by the combined diseases which affect the heart.

Cancer was responsible in the past year for approximately one thousand deaths per month. The death rate from cancer has been steadily mounting. It will continue to mount unless we do something to control its progress. We use the word "control" deliberately. We cannot hope to eradicate cancer in our present state of knowledge. Only when our present knowledge has been enormously increased by research will eradication be possible. We can hope to control

it if our present limited knowledge of the disease is intelligently applied. We, during our time, must depend upon the presently known information.

What is cancer? Briefly stated, it is simply this. Clinically speaking, cancer is at first a local disease. If cancer in an accessible region of the body is recognized early, before it has spread to distant parts, and if treatment is promptly applied in the form of surgery or, in suitable cases, radiation, the patient can be cured. If, on the other hand, through ignorance or indifference, such a case is not recognized early, or if, recognized, early treatment is neglected, no power on earth can cure it.

We can truthfully state dogmatically that no form of treatment except surgery and radiation has ever been proved to have curative value. The curative value of these measures is strictly limited to early cases. Why then has this knowledge not been intelligently applied?

The intelligent application presupposes that each case will be recognized early by the doctor who first examines it. This will be possible only if the victim of the disease is aware of the possible significance of the early signs which he himself or herself can recognize and will at once consult his physician. The intelligent application of our knowledge is thwarted by the fact that the overwhelming majority of our people are ignorant of the meaning of these early warning signs. We can make progress only when the people have been enlightened. Tremendous as this task of enlightenment is, a large number of men and women in Canada are convinced that it can be accomplished by persistent organized effort.

With this end in view, the Canadian Society for the Control of Cancer has been established. It proposes to build up a membership in every part of Canada composed of men and women who are willing to aid in bringing about a widely disseminated knowledge relating to the early manifestations of cancer. The Society has secured the cooperation of the Canadian Medical Association with its organized branches in every community. The organized medical profession has undertaken to provide speakers who will instruct groups of members of our Society and their friends whenever we request them to do so.

They have also undertaken to carry on among themselves, the Canadian doctors, an intensive program directed at making each of them keenly alive to the necessity of early diagnosis and prompt adequate treatment in all cases of cancer.

In developing the Society we are appealing to men and women in every community who are anxious to help to enrol members of the Society among those who now constitute the membership of existing organizations. Some may be closely associated with a church organization or an auxiliary to a church. Others can exert influence upon the members of a service club, a fraternal society, an industrial or a social

organization. Within each of these a unit of the Canadian Society for the Control of Cancer can be organized.

Each member can aid in the educational campaign. He can aid in extending our knowledge regarding cancer by contributing toward the support of Canadian workers in the field of research.

No matter how modest may be the estimate of the individual of the value of the aid which he can give, his help, when combined with that of others like him, will constitute a tremendous weapon in controlling cancer.

J. S. McEACHERN, *President,*

Canadian Society for the Control of Cancer.

Special Articles

INSULIN THERAPY IN THE FUTURE OF PSYCHIATRY*

By DR. MANFRED SAKEL

Vienna

It has been my hope since the development of the pharmacological shock treatment of major psychosis that it will prove to be an important factor in some of the coming changes in psychiatry. I refer particularly to the desirable tendency for psychiatry to come closer to medicine and for medicine to become more closely associated with psychiatry. Both have everything to gain by such an evolution. The psychiatrist has always had rather an isolated position in medicine as exemplified by the term "alienist". His patients have been considered only as a group to be kept away from others, and the psychiatrist has been looked upon as the custodian of such cases, protecting them and the public from their follies.

There are many reasons, both historical and current, that might lead the laity to adopt such a viewpoint, but I wish to mention some of the reasons why, in my opinion, this isolation did exist within the medical specialties. Is it not that psychiatrists sometimes forget and that others, perhaps, have never thought of mental disorders of various kinds and classifications as merely symptoms of disordered function? For many years we have ceased to consider fever, jaundice, tachycardia or colic as distinct diseases. In the face of such symptoms we now look deeper, for disorder due to infection, or to the functions of the liver, blood, heart and hollow viscera. We psychiatrists have carefully classified symptoms, but only in some cases have we gone behind these symptoms to find their origin. We know today that we must consider the mind and its disorders as manifestations of the function and dysfunction respectively of the organism as a whole.

There is nothing new in this tendency to take obvious things for granted and to postpone logical thought or delegate this to those so inclined. For many centuries we were satisfied

to accept life itself without questioning and without inquiring as to its beginnings, variations and potentialities. Now we have some desire of understanding how life began, of its continuation and limitations. We may look forward to a similar search and understanding of the mind and even the variations in the individual personalities.

Early in my studies of mental disorder I began to think of every experience and emotion of individuals as expressions of function. The usually accepted ideas concerning drug and alcohol addiction did not satisfy me, nor had they led to much success in therapy. It seemed evident that the toxins these patients had been subjected to had made definite changes in their personality. Attempts were made to correct these pathophysiological metabolic changes by the use of insulin and with some success. Since then we have learned that profound changes in personality may result from pharmacological shock therapy.

Here then we have an artificial biochemical alteration producing changes in personality. We ask ourselves the question; how are these changes brought about? Let me call your attention to certain features of mental disorder in general. We may first think of what constitutes mind as we know it. Its manifestations in the form of thoughts, emotions and actions are the result of an organization and classification of many simple sensations. There are possibilities in such organization for changes in quality as well as degree. With no sensation we can have no mind, yet clinically we deal with severe disorders of function and various degrees of mental deterioration when all the primary sensibilities are intact. The patient may feel, taste, smell, hear, and see and yet be unable to correlate some or all of these elements into more complex systems, or there may be inadequate emotional responses showing that there has been a change in the quality of such organization. We may now consider the possibility that this organization or integration called *mind*, and the higher associations called *personality*, are recent ontogenic acquisitions. This, together with its continuous activity, renders mind susceptible to pathological change more readily than older structures and mechanisms. Finally, it would appear clinically that

* An address given before the Psychiatric Section of the Montreal Medico-Chirurgical Society, May 19, 1938.

disorders in one portion of the mind tend to create disturbances in function throughout the whole. In the normal there appears to be a dominant characteristic personality that is carried through all the ever changing experiences. Any pathological change tends to assume this dominant position. This may be compared to a house in which one unclean room will create an odour that will permeate the whole structure. Therapeutically, a remission results when the room is completely closed, a cure results when the room has been completely cleaned.

Insulin hypoglycæmia produces many changes in the vegetative nervous system, probably blocking off those centres in the mid-brain concerned with brain metabolism. It creates a severe sugar hunger in the individual cells; the resulting defense mechanisms are stimulated. Water metabolism in psychosis, about which we know so little, may be a factor in that some of the sudden changes in patients may be related to the dehydration and hydration phases. The fact that, clinically, the treatment often effects contrasting results in one patient, such as changing a manic phase to a depressed phase, while producing an apparently opposite effect in another, such as activating an excited state in a stuporous patient, suggests that different malfunctioning, perhaps malnourished cell systems are being acted upon. I am certain that the psychological and physiological accompaniments of fear have nothing to do with remissions seen in patients. Fear has no place in the treatment of the more profound mental disorders.

I have only touched upon a few of the many problems concerned in the pharmacological shock treatment of psychosis. However, I think it has become apparent that in the solution of these problems psychiatry will be brought to medicine and medicine will come to psychiatry.

DIET AND NUTRITION VITAMINS IN INFANCY AND CHILDHOOD*

BY FREDERICK F. TISDALL

Toronto

VI.

Experimental work with animals gives evidence that there are no less than 15 different vitamins. However, only 7 of these are well recognized—vitamin A, three members of the vitamin B complex, namely, B₁, riboflavin, and nicotinic acid, and vitamins C, D, and E.

Vitamin A.—A complete or marked lack of vitamin A results after some 2 to 4 months in the development of an eye condition called

xerophthalmia. In this disease the eye has a peculiar ground-glass appearance and corneal ulcers appear. If the patient is not treated with vitamin A the ulceration will proceed, with final destruction of the eye. Fortunately this condition is extremely rare in Canada. In the last million attendances at the Hospital for Sick Children, Toronto, only one case of xerophthalmia has been noted. A partial lack of vitamin A causes the condition known as night-blindness, that is, a patient is unable to adjust his vision to changes in light intensity, such as occur when going from a bright room to a poorly lighted room. With a lack of vitamin A the columnar cells of the mucous membranes throughout the body gradually become squamous in character. This interferes with their normal function.

The exact vitamin A needs of both children and adults are unknown. However, of all the vitamins vitamin A is the most widely and abundantly distributed. It is present in large amounts in the fat of milk (milk, cream and butter), coloured vegetables, such as carrots, spinach and tomatoes, and in egg, liver and kidney. There is no evidence to indicate that if the child is receiving a reasonable diet it will suffer from a lack of vitamin A, or require additional amounts in concentrated form.

Vitamin B₁.—The story for vitamin B₁ is entirely different from that for vitamin A. Vitamin B₁, or thiamin, is widely but not abundantly distributed in foods. Our most concentrated food source is wheat germ, which, unfortunately, is carefully separated in our modern milling process, the white flour being reserved for human consumption and the germ used largely in animal feeds. This constitutes a great loss of this vitamin to the Canadian people. Another excellent source of vitamin B₁ is yeast, which of course can hardly be considered an ordinary food. We get vitamin B₁ in small amounts in milk, egg-yolk, liver, kidney, in many vegetables, particularly peas and beans, and traces in many fruits. Due to the wide use of finely milled flours and sugars 35 to 45 per cent of the calories ordinarily consumed by the older child and adult contain practically no vitamin B₁. In addition, as vitamin B₁ is water soluble, investigations show that a large proportion of this vitamin in vegetables may go into solution in the cooking water and be discarded. For these reasons, one would expect some evidence of a lack of vitamin B₁ in the Canadian population.

A lack of this vitamin results in the disease beriberi or polyneuritis. This disease is rarely seen in Canada. One of the prominent symptoms of a lack of vitamin B₁ in animals is loss of appetite and the development of atony of the intestinal tract. There is evidence that in some instances these symptoms occur in human beings as a result of a deficiency of this vitamin. Also it has been found that with two

* This is the sixth in the series of articles on Diet and Nutrition, prepared under the auspices of the Association's Committee on Nutrition. The previous articles can be found in the *Journal*, 1938, 38: 277, 387, 491, 586; 39: 76.

groups of children living in an orphanage and both fed exactly the same diet, which according to our Canadian standards was a good one, the daily addition of a small amount of vitamin B₁ concentrate to the diet of one group resulted in an increased gain in weight in the children in that group. This would indicate that possibly the diet without the addition of the vitamin B₁ did not contain the optimum amount of this vitamin.

The physician should watch carefully his patient's diet from the standpoint of its vitamin B₁ content. Although vitamin B₁ is not present in high concentration in milk, this food is really an important source of it owing to the relatively large amounts of milk consumed. To illustrate this point, one and one-half pints of milk supply approximately 200 international units of vitamin B₁, with the total daily requirements 400 to 500 units. Vegetables should be used freely and the cooking done with a minimum amount of water so that the loss from solution in discarded cooking water is reduced to a minimum. The use of whole grain cereals, egg, liver and kidney will also help to supply appreciable amounts of vitamin B₁.

Vitamin B₂, or riboflavin.—In 1926 it was demonstrated that what was then called vitamin B consisted of two parts, and one was called B₁ and the other B₂. Experimental work since that time has shown that vitamin B₂ really consists of a number of different components, and of these two have been isolated and are well known, namely, riboflavin and nicotinic acid.

Riboflavin is necessary to maintain life in animals, and a lack of it results in lack of growth and a premature ageing of the skin, with loss of hair. Unfortunately, the exact place of riboflavin in human nutrition has not been demonstrated, but there is no doubt in the minds of the investigators who have worked with this food substance that if it were lacking in the human diet serious results would follow. Its distribution follows to a degree that of vitamin B₁, although in many foods it seems to be more abundant. If a diet contains an adequate amount of vitamin B₁, it is probable it also contains an adequate amount of riboflavin.

Nicotinic acid.—This acid has been known to chemists for over seventy-five years, yet no one suspected that it was of any importance in nutrition until September, 1937, when Elvehjem reported that the administration of nicotinic acid cured a disease in dogs known as black tongue. Following this work by Elvehjem, Spies in November, 1937, reported that the administration of nicotinic acid to patients with pellagra resulted in spectacular cure of the mucous membrane lesions and a gradual improvement in the whole condition of the patient. This work has been amply confirmed by many workers. Fortunately, pellagra is practically unknown in Canada.

The concentration of nicotinic acid in foods has not been determined, but this vitamin is probably present in relatively good concentration in yeast, wheat germ, liver, milk and eggs.

Vitamin C, or ascorbic acid.—A lack of vitamin C results in the development of scurvy. The most prominent pathological change which occurs in the body is an increased permeability of the capillaries so that there is a tendency to bleeding. The disease is rarely seen under 6 months of age, even in those children who do not receive any anti-scorbutic. The first symptom of scurvy is pain or tenderness of the legs when the infant is handled. This is due to hæmorrhage which has occurred underneath the periosteum at the ends of the long bones. The pain may be so great, with resultant lack of movement, that a mistaken diagnosis of paralysis of the legs may be made. Also the diagnosis of scurvy is sometimes confused with that of septic arthritis. If any of the teeth are through, hæmorrhages frequently occur at the junction of the teeth and gums. Also blood may be found in the urine, stools, skin and mucous membranes.

The vitamin C content of cow's milk is so low that it cannot be depended upon as a source. Accordingly, every artificially fed infant should receive vitamin C in the form of either orange juice or strained factory canned tomatoes. It was formerly thought that as scurvy rarely developed under 6 months of age it was not necessary to administer vitamin C until about 3 months of age, but estimations of the vitamin C content of the blood of young infants indicate that it is advisable to start orange juice or strained canned tomatoes during the first month of life. The amount should be rapidly increased to 1 ounce of orange juice daily or 2 to 3 ounces of strained canned tomatoes. This should be continued throughout childhood.

Vitamin D.—A lack of the sunshine vitamin D results in the development of rickets. In observations undertaken in Toronto it was found that 50 per cent of infants who did not receive vitamin D during the winter months developed some evidence of this disease, approximately one-half of these in a severe form. Enlarged abdomen, softness of the bones of the skull, delayed closure of the fontanelles, delayed dentition, loss of muscular tone, and deformity of the long bones and ribs are too well known to require any detailed description. As rickets starts at an early age, that is, in the second and third month of life, it is advisable to give every infant, breast-fed or otherwise, some vitamin D, beginning at 2 to 3 weeks of age.

There are available at the present time numerous biologically tested cod liver oils, high potency fish oils, and viosterol. The dose of vitamin D required is approximately 500 international units daily, which are furnished by 1 teaspoonful of most of the cod liver oils available in Canada, or by 3 to 5 drops of the high potency fish oils, such as those obtained from

the percomorphum group. Three to 5 drops daily of viosterol are also sufficient.

The administration of vitamin D should be continued throughout the year, with the exception of the two to three summer months when the infant can be out-of-doors and his whole body exposed to the sun's rays. It should be kept in mind that the need for vitamin D does not stop at the end of infancy but continues throughout the whole of childhood.

Vitamin E.—The importance of vitamin E in the nutrition of the child has not been demonstrated. However, vitamin E is widely distributed in many foods, so it is quite unlikely that children do not receive an adequate supply of this vitamin.

One should keep in mind that a lack of any one of the above mentioned vitamins does not necessarily result in the development of a well marked disease. It has been shown that if the optimum amount of these vitamins is not being consumed resistance to disease is definitely lowered. It is therefore essential to see that children receive adequate amounts of the recognized vitamins. This can be accomplished if the child consumes each day a pint to a pint and a half of milk, one egg, two vegetables besides potato (cooked with as little water as possible) and some raw fruit or raw vegetables. In addition, except during the three summer months, some source of vitamin D should be administered daily.

Men and Books

EARLY VACCINATIONS IN BRITISH NORTH AMERICA

BY R. CAMERON STEWART, B.Sc., M.D.

Montreal

Edward Jenner^{1, 2, 3} vaccinated his first case in 1796. Long consideration of certain facts under his notice as a country doctor and naturalist, and a reasonable assurance as to the expected result, preceded the momentous test. The details of this event, the reasoning that led up to it, the results that followed, have often been described. It was commonly believed among dairy farming folk that milkers and others in contact with cattle, who became accidentally infected with a disease called cowpox, were afterwards immune to small-pox. A few artificial inoculations^{2, 7} with protection in mind had already been tried in England and on the Continent in Holstein, but it is unlikely that Jenner knew of these attempts. He, in any case, made a fresh and original approach to the subject, carried through his ideas to a successful conclusion, and introduced a measure of the most far-reaching importance, both in its actual benefits and its future implications.

Jenner^{2, 3} was a kindly man, with many friends, conscientious in his professional work, an able physician; a lover of country life, poetry, and music; and a naturalist of no mean distinction. He had already made important observations on such diverse phenomena as the pathology of angina pectoris, the habits of the cuckoo, and the hibernation of animals, and afterwards wrote on the migration of birds. As a young man he had served as a surgeon apprentice before going to London to study under John Hunter. He had helped to arrange the zoological specimens collected on Captain Cook's first voyage, and was recommended by Sir Joseph Banks as naturalist for the second voyage. Jenner, however, preferred to take

up country practice at his old home near Berkeley in the west of England, about thirty miles from Bath. Thus qualified by tastes, training and environment, he carefully worked out his great discovery. This was given freely to the world in a small book or pamphlet,¹ "An Inquiry into the Causes and Effects of the Variolæ Vaccinæ", published in 1798. Clearly and simply written, beautifully printed and illustrated in colour, this little epoch-making work and some others by Jenner on the same subject are among the valued treasures of the Osler Library in the Medical Building at McGill University.

Small-pox was such a menace and its control so great a problem that reports of the new method aroused widespread interest. Here and there, in Europe, and elsewhere, favoured individuals obtained small quantities of the vaccine from Jenner and his friends, or, profiting by his description of cowpox, in a few cases directly from locally infected cattle. Material from these centres of supply became available for the vaccination of many scattered groups. The results when instructions were duly followed being generally good, the practice gradually spread, although naturally not without discussion, controversy, and sometimes definite opposition. It began to be widely carried out in the British army and navy at home and abroad.^{2, 3} Dr. J. De Carro,² a Swiss graduate of Edinburgh living in Vienna, Austria, did the first vaccinations on the Continent in 1799, and others were done shortly afterwards in the neighbouring countries, often with official support. Philanthropic people became interested, and the comparatively simple little operation was sometimes performed by non-medical men and women as a measure of public welfare. Jenner conducted a voluminous correspondence,^{2, 3} and gave advice and vaccine gratuitously to the many who asked, making no attempt to control his discovery for private gain. This beneficent generosity was

later recognized by the British Government, and rewarded by grants of money. Few medical procedures have stood so well the relentless test of time. The experience gained in its use and the practical success attained against smallpox have been important factors of encouragement in the attack on other diseases along the same lines. Among the fortunate few to obtain early supplies of vaccine were men in the United States and in the British American colonies of Newfoundland, Canada, and Nova Scotia. The names of those who here introduced the new procedure, a few brief notes about them, and some of the circumstances of the time may not unfittingly be recalled.

Newfoundland probably had the distinction of receiving the first vaccine to be sent out of England. The Rev. John Clinch, M.D., was serving there as an Anglican missionary when he received a small quantity of lymph and used it to vaccinate his nephew, about 1798. Clinch and Jenner had been schoolmates together at Cirencester, and afterwards fellow students under John Hunter in London, and when the former came out to Newfoundland in 1775⁵ the early friendship was not broken. He took up medical practice at Bonavista, which many think was Cabot's landing place in 1497, and moved in 1783 to Trinity, the old settlement elustering about the splendid harbour discovered by Cortereal on Trinity Sunday, 1500. Here Dr. Clinch lived for many years as physician and clergyman, receiving ordination in England in 1787. He also acted as Justice of the Peace and later as a Judge of the Surrogate Court. It was not unusual in those days for churchmen and physicians to be made magistrates, both in England and abroad, and thus to take part in local government. Jenner held a commission at Berkeley. The active useful public life of Dr. Clinch closed in 1819,⁵ and he was buried in old St. Paul's Church, where he had ministered so long. Such was the man whom Jenner addressed as "My Dearest Friend" in a letter³ of 1789. Reference is made to George Jenner, the writer's nephew, who had accepted an offer by Clinch of some position or appointment in Newfoundland. This was presumably the Rev. G. C. Jenner,^{5, 6} who afterwards, in 1795, became the Church of England clergyman at Harbor Grace, and is probably mentioned in a letter³ from Clinch to Jenner in 1796. The protection following "Jennerian inoculation", evidenced during a small-pox epidemic at St. John's, is noted in a later letter³ from Clinch to his friend. Reference is made to Dr. Clinch's use of vaccine, by the late Rev. Canon Lockyer, an authority on the local history, under the heading "Trinity Notes" in the St. John's *Evening Telegram*, July 5, 1924.¹² The exact date is not given, but their close friendship makes it altogether likely that the vaccine was forwarded by Jenner himself to his old associate soon after its success had been established, and explains its

very early use in the distant fishing community, Britain's oldest colony.

The United States obtained its first supply of vaccine, so far as is known, in the summer of 1800. Dr. Benjamin Waterhouse,^{2, 7, 8} Professor of the Practice of Medicine at Harvard, was an interested reader of Jenner's description of cowpox and the early vaccinations. He wrote a short article² on the subject in the *Columbia Sentinel* in 1799. Next year he received a little lymph from Dr. Haygarth, of Bath, and in July vaccinated several of his children. This same summer some reached Dr. John Crawford,⁸ of Baltimore, from Dr. John Ring, of London, and about this time or shortly afterwards vaccinations were also being done by Drs. Elisha North,⁷ of Goshen, Connecticut; James Smith, of Baltimore; David Hosack, of New York; John Redman Coxe, of Philadelphia; and James Jackson, of Boston. So rapid was the progress of the practice that as early as 1802 a Vaccine Institute^{7, 8} was founded at Baltimore by James Smith.

Canada and Nova Scotia, then separate colonies not yet united by Confederation, had meantime obtained independently their own supplies direct from England.

To Col. George Landmann,⁹ an officer of the Royal Engineers with wide interests and good scientific training, were due the first vaccinations in this country. While at Quebec in November, 1801, he received a letter describing the use of the new virus, and drawings of the various stages of reaction. Enclosed, between two small pieces of plate glass, was a little of the precious yellowish lymph. Captain Backwell, a brother officer in the Royal Engineers, previously stationed at Amherstburg, Upper Canada, was then at Quebec with his wife and two children. The latter were promptly vaccinated, and material from these cases was transferred to others, thus preserving the activity of the agent. News of the novel procedure attracted wide attention, as physicians came even from the United States to secure a supply of vaccine. An account⁹ of this incident is given on page 236 of the second volume of Col. Landmann's "Adventures and Recollections". The author came to Canada, by way of Halifax and New York, in 1797 and returned to England in 1802. He travelled extensively and his book includes vivid descriptions of varied aspects of colonial life.

The date of the vaccinations thus performed on little Elizabeth Catherine Backwell and her baby brother Frederick can be determined, to within a few days, by a happy coincidence. The letter with the vaccine was received by Col. Landmann within an hour or so of the baptism of the children by the Rev. Salter Jehosaphat Mountain, then Deputy Chaplain to the Garrison, later a Bishop. Dean Crowfoot, of Quebec, has been kind enough to look up the Church of England records, and there clearly written in

the old Register, are the entries of the two baptisms on "November the twenty-eighth, in the Year of Our Lord, one thousand eight hundred and one". The vaccinations were carried out on that day or very soon after.

Nova Scotia was not far behind. Dr. Joseph Norman Bond,^{4, 10, 11} of Yarmouth, received some lymph in the spring of 1802 from his brother in Bath, England, a lawyer and a friend of Jenner's. Dr. Bond vaccinated his own little baby, who later grew up to be a physician himself, Dr. Joseph Blackburn Bond. The results were such that others were then done. Dr. Bond was a good example of the type of medical man who rose to prominence in many colonial communities. Of English birth and education, he arrived at New York during the Revolution. Joining the British army, he served as an assistant surgeon. When the war ended he came to Nova Scotia and joined the great Loyalist settlement at Shelburne, the largest for a time in the colony. About 1790 he moved to Yarmouth. Here he practised with success, and was honoured with public office: magistrate, colonel of militia, collector of customs, and sheriff. This account of his first vaccination and brief summary of his long and worthy life is based on information contained in a letter¹⁰ written by his granddaughter, Mrs. Maria J. I. Thorburn, to Dr. Peter H. Bryce, of Ottawa, in 1921, and in Dr. D. A. Campbell's "Pioneers of Medicine in Nova Scotia".¹¹

A medical missionary in Newfoundland, a military engineer in Canada, and a physician in Nova Scotia are thus to be credited with the introduction of vaccination into British North America.

Acknowledgment is made, with thanks, of courtesies extended by Dean Crowfoot, of Quebec, who supplied copies of the baptismal certificates of Elizabeth and Frederick Backwell; by Dr. W. W. Francis, Librarian, Osler Library, McGill University; by Dr. D. C. Harvey, Halifax, Archivist of Nova Scotia; by Dr. H. M. Mosdell, Secretary for Public Health and Welfare, Newfoundland and by Mr. R. B. Herder, of the St. John's *Evening Telegram*. Among the factual sources used were the following, the more specific references being indicated by numbers.

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Association Notes

The Annual Meeting

The Annual Meeting of the Association, held in Halifax from June 20th to 24th, was an unqualified success. The "weather man" was gracious and the visitors were enabled to take advantage to the full of the many out-door attractions that had been provided. Halifax is preeminently an "out of doors" city and was at its best. Every one, we are satisfied, went home pleased. The attendance was excellent, 585 medical men, 340 ladies, and 118 children being registered. The hotel accommodation being somewhat limited, so far as any one individual hotel was concerned, the visitors had to be accommodated in several institutions, hotels and other, but this was not really a great disadvantage, particularly as all the business and scientific sessions of the Association were held in one convenient place, the Nova Scotian Hotel. The authorities of Dalhousie University kindly placed at the disposal of the Housing Committee the beautiful Shirreff Hall, where rooms and breakfast were provided.

The Executive Committee met on June 17th and 18th and prepared the material for discussion and action on the part of the General Council which met on June 20th and 21st. Many important matters were disposed of, more extended details of which will be published later. We had hoped that the Halifax Meeting would see the complete consummation of the Federation Scheme whereby the various provincial medical associations become Divisions of the National Organization. However, this did not eventuate. Nevertheless gratifying progress was made and seven of the nine provincial bodies are now Divisions of the larger Association. Manitoba and New Brunswick so far have not completed the final arrangements.

A Constitution and By-laws applicable to divisions, as previously published in the *Journal*, was adopted with minor changes and a committee was empowered to effect consolidation of this Constitution and By-laws as adopted with that of the Canadian Medical Association as presently existing.

The Association's Study Committee on Cancer, of which Dr. J. S. McEachern, of Calgary, is the energetic Chairman, reported that a sub-committee, with Dr. Roscoe Graham at its head, was preparing a booklet on the early signs and symptoms of cancer, of which a copy was to be placed in the hands of every doctor in Canada who desires to have one. The Committee had been also empowered to set up a Canadian Society for the Control of Cancer, and the organization has received its Articles of Incorporation from the Federal Government and is now a legal body. The proceedings have reached the stage when an active canvass for membership can be undertaken.

It was announced that the International Hospital Association, representing nearly fifty countries, together with the American Hospital Association, will meet in Toronto next year. It is gratifying to learn that our Associate Secretary, Dr. Harvey Agnew, is the incoming president. We congratulate him on this well-deserved honour.

The Code of Ethics of the Association, as drafted by the late Dr. D. A. Stewart, of Ninette, Man., and subsequently modified by Dr. Ross Mitchell and his committee, and the Executive Bodies was adopted.

The general sessions of the Association were held at the Nova Scotian each morning in the Ball Room and the various sectional meetings in the afternoons, beginning on June 22nd. This arrangement worked out very satisfactorily. The following Sections were represented—Anæsthesia, Medicine, Ophthalmology and Otolaryngology, Pædiatrics, Radiology, Surgery, Urology. The attendance at all of these was good.

The various luncheons proved popular and the guest speakers were well chosen. All the topics dealt with were informative and excellently presented. On Monday the guest-speaker was Dr. J. S. Martell, Assistant Provincial Archivist, Halifax, who spoke on "The Melting Pot", particularly as concerning Nova Scotia, but with some reference to other parts of Canada. His address was most instructive.

On Wednesday the speaker was the Hon. Angus L. McDonald, Premier of Nova Scotia, who made a strong plea for the development of a stronger sense of brotherhood between the various provinces of Canada. At no stage of our development were we more in need of unity of thought and action. The times were dangerous and should provoke our best effort. On Thursday the address was given by the Rev. Stanley Walker, President of King's University, who, in a very able effort, enunciated the general theme that Medicine, in common with other sciences, needed a free atmosphere, and an intelligently sceptical frame of mind to prosper. He drew parallels from the history of the development of political, juristic and constitutional ideas, and then proceeded to run through the History of Medicine from Homer to about the eighteenth century, with an odd reference to the nineteenth, to show that the same needs were obvious for medicine, and that when authoritarianism had been most developed, as in the middle ages (outside Spain), medicine had stuck in the mud of obscurantism and superstition. The Friday's talk was by Dr. Carleton Stanley, President of Dalhousie University, who took as his topic "Thinking past the profession".

The Annual Meeting, held on Wednesday evening, was a striking and colourful function,

at which the ceremonial of the Association was duly honoured. The new president was installed by his predecessor, Dr. T. H. Leggett, of Ottawa, and the visiting delegates were welcomed. Sir Humphry Rolleston, Bt., the official delegate from the British Medical Association, and this year's Osler Orator, was made an Honorary Member of the Canadian Medical Association, and ten medical men from various parts of Canada were made Senior Members. Dr. J. S. McEachern, of Calgary, was presented with the Starr Gold Medal for distinguished service to the Canadian Medical Association.

The reception of the members and guests by President and Mrs. K. A. MacKenzie, held immediately after the Annual Meeting, was a delightful function and was followed by a Dance and Bridge.

A Golf Tournament was held at Ashburn, and in the evening of Friday, June 24th, a dinner was held at the Ashburn Golf Club, at which Dr. W. Alan Curry presented the prizes. The winners were: (1) The Ontario Cup—best net, Dr. C. W. Holland, Halifax; (2) runner-up, Dr. C. M. Jones, Halifax; (3) low gross, Dr. L. M. Morton, Yarmouth; (4) runner-up, Dr. W. G. Colwell, Halifax; (5) hidden hole, Dr. P. A. MacDonald, Halifax.

The thanks of the Canadian Medical Association are extended to all who contributed to the success of the Meeting and to those who so graciously extended their private hospitality, thus rendering the stay of the visitors full of delight. Among so many it is hard to make selection, but, without intending to make invidious distinction, we may be permitted to acknowledge the kindness of His Honour, the Lieutenant-Governor, the Honourable the Premier of Nova Scotia, His Worship the Mayor of Halifax, the Guest-speakers, President and Mrs. K. A. MacKenzie, Dalhousie University, the Department of Public Health of Nova Scotia, the Chairmen and members of the many Committees, and of the ladies who so well looked after the pleasure of the visiting ladies and children. The entertainment provided was lavishly extended and gratefully received.

The Valedictory Address of the retiring President, Dr. T. H. Leggett, of Ottawa, was delivered on Thursday afternoon, June 23rd, and was as follows.

Valedictory Address by Dr. T. H. Leggett, Retiring President of the Canadian Medical Association

One cannot hold the high honour which has been my privilege this past year without feeling a sense of heavy responsibility toward our conception of duty as a national body in the present troubled world. I would consider it the greatest achievement of my life could I express my thoughts that they might provoke commensurate action, that they might arouse the conscience of every member of our profession to the vital problems before us, that they might assure the cooperation of all members in solving those problems—problems created by

the rapidly changing relationship of our profession to the public and to community life.

Seventy years ago, in September, 1868, Sir Charles Tupper, then The Honourable Dr. Charles Tupper, in opening the first regular meeting of The Canadian Medical Association in Montreal, welcomed his colleagues as "members of a profession the most noble, the most unselfish, and the most influential of any secular profession or calling."

In those days, as also today, the requirements of social justice—justice pertaining to the ordinary or natural condition of human living for the citizen—were five in number, *viz.*, adequate food, clothing, housing, fuel and care of the sick. The physician supplied the last requirement in the shape of medical care, necessary drugs and instruction in home nursing; as well as by advising upon the proper use of the other four requirements in the prevention of illness and maintenance of the highest known standard of health. This was a large share in the community effort. The remaining complement of complete social justice was largely effected by neighbourly activities carried out in a general way. History has now passed judgment upon those times, and we find that Dr. Tupper's remarks were quite apt; and no citizens, because they could not pay, were denied the bountiful share of social justice so generously donated by the physician.

Seventy years have passed. In this day, with electricity, the telephone, the automobile, the aeroplane, the radio, and television being born into our homes, no one will challenge the statement that events are moving in the world of today faster than ever before. The unceasing dynamic developments of rapid changes in our very existence, in our modern methods of living, and in our conceptions of the relationship of the individual to the State, all make for much confusion of understandings, and give rise to some concern in the course which we may choose to follow on the way to our ultimate objective. We have cause to be uneasy.

Today the requirements of social justice have become the demands of social justice. The blessings of benevolent neighbourly activities have become the legal and specific right which the citizen demands from the State; and the services which were so willingly donated by the physician now carry a demand for payment if not by the individual, then by the State.

Owing to these fundamental changes the relationship of our profession to the community is taking a vastly different form, and we must adapt ourselves hopefully and beneficently to this altered and continuously altering relationship. We are evolving in the natural course of events what will without doubt become a highly developed lay medical administration in all branches of our work. In some the State is, and will remain, the larger partner, as in the administration of hospital care for tuberculosis and mental cases. The hospitals for this work have full time medical staffs. The State is an influential partner in the administration of care of workmen's compensation cases, though the treatment of these cases still rests entirely with the medical practitioner. In other fields voluntary lay medical organizations are formed for administrative purposes. Some of these organizations are national in character. We are realizing more and more that the health of the people is a national problem. We are thinking and acting nationally and internationally in the matter, with the advancement in this trend more rapid of late, as witness the studies of the Health Committee of The League of Nations, in epidemiology, nutrition, etc.

In the field of nutrition we note nowadays in practically every country a rapidly growing consciousness in the public mind of the importance of proper nutrition. Our Committee on Nutrition has been holding a series of public meetings across Canada with addresses suitable for lay medical audiences by outstanding scientists of this continent and Great Britain. The Dominion Council on Nutrition is now organized under the Department of Pensions and National Health, and held its first meeting in Ottawa two months ago.

The Canadian Society for the Control of Cancer has been launched as a national body by our Association. The Grand Council, consisting of practically equal numbers of medical men and laymen, will be supreme in the Society.

Medical research in Canada really assumed a national aspect when the efforts of the past year and a half in organization were brought to fruition with the conference of research workers from all over Canada, and resulted in the launching of the Associate Committee on Medical Research under the aegis of The National Research Council. The objective is the coordination of all activities in medical research and the correlation of the results, thus assuring more systematic and effective effort.

Now all these accomplishments bring notable changes in our economy, and speed up the already rapid advances being achieved in the medical sciences, at the same time making their application to the treatment of disease an increasingly involved and costly process, giving grave concern to the heads of families, and making the problem of paying these costs more and more urgent of solution. The Public Health Services—sanitation, the prevention of communication of disease, and general health education—have for centuries been a responsibility of governments. Within the past month the Minister of Pensions and National Health has announced the establishment in his department of a Health Education Branch to conduct a campaign reaching all parts of the country so that "no part will be more informed than another". He states also that "there is growing throughout every country a greater consciousness of the responsibility of the State towards its citizens in the matter of health."

But the actual care of the sick has through the ages largely been left to seek out its own salvation. In Canada 70 per cent of our hospitals for acute diseases are still under voluntary direction, and the care of the sick in the homes is entirely voluntary. With so much public concern over the increasing costs of these services, lay medical organization is taking hold and striving to solve the problem of paying these increasing costs. By budgeting beforehand and administering prepayment medical services and group hospitalization plans the large body of our citizens may perhaps be satisfactorily provided for, but much depends upon the disposal made of our responsibility to one class of citizens—those in the lower income brackets. This will have a far-reaching effect on our whole economy, and we must be careful to give most matured consideration to this class in our planning. If we give noble leadership toward a successful solution of this problem, we as physicians, may fortunately retain our proud and influential position in community life.

Our citizens may be divided in a general way for purpose of medical care into three classes:—(1) the well-to-do; (2) the medium class, largely the salaried class and the more highly paid wage-earners, and (3) the class in the lower income brackets. It may be presumed that the first class can take care of itself; the second likewise, provided they are given a lead toward voluntary cooperative group organization for securing medical services and hospital care. The third is definitely a public responsibility and the State must accept it. Here we need all the tact and good judgment of which statesmanship is capable. But our governments, legislating for the State, reflect only our ideas expressed as the will of the majority.

The State can discharge its responsibility in this case in only one of two ways—either by paying for these services direct (State Medicine) or by assuming responsibility for earning power for the worker sufficient to pay for these things himself. Direct payment by the State for these medical services is unwholesome, undermines the self-respect in the individual, encouraging him to demand from the State more and more of the things he should supply for himself. Surely it is a natural law that every citizen is entitled to gainful occupation throughout his working life-span, sufficient to supply the requirements for human living for himself, for his

dependents to earning age, and for his retirement in old age. The State is entitled in return to assurance that the citizen will seek out and diligently pursue a gainful occupation throughout his working life. Must we have the indigent always with us? Not in a conceivably proper organization of society. Any unavoidable gap in the working life span of the citizen owing to illness may be filled through unemployment insurance on the plan of prepayment for the requirements for human living. The costs of illness should be included in the above. They are comparatively easy of administration by means of deductions of these items at the source. Our Workmen's Compensation Acts have pointed the way in this regard, and the worker thus joins in the contributory plan of prepayment for his medical services, which he can command with the preservation of his self-respect, knowing he has earned and paid for them himself. This condition could undoubtedly be realized, based upon a Dominion-Provincial relationship with the powers and responsibilities of each government clearly defined. Governmental efforts, purely paternalistic, are satisfying morsels for the weak-minded, not for those of individual character, not for those who love freedom—freedom to enjoy that solid economy for the able-bodied citizen, of self-support through his own production of useful goods and services.

The State's consciousness of Social Justice is the reflection of the collective consciousness of the individuals comprising the State. In the uncertain years following 1929 the State was forced to take over the administration of social justice as emergent circumstances demanded, and thus "Relief" was born. In the confusion of emergent relief we have discovered influences in many directions undermining the self-respect of the individual citizen. We have found in our method of relief unfortunate encouragement of unemployment; and we have learned that unemployment, when prolonged, creates unemployables. Let us hope social justice will some day demand that the State cease thus to undermine the self-respect in the individual, that the State provide, not the five requirements of human living for the individual with no effort on his part; but that it provide equal opportunity for all by removing all obstacles created by the organization of society, toward making these things available to the citizen by his own effort. Then and only then is society functioning properly. Then and only then can we expect the citizen to see clearly his duty to the state; and the state can enact that the citizen accept his own responsibility in following a gainful occupation throughout his working life span.

Out of all this collective action will come. Will it be collective action for cooperation and coordination of effort in the building of sound minds and bodies in our citizenry, and the persistent strengthening of our moral framework? or will it be collective action for confusion, for conflict, for disruption of the moral forces for good, and the undermining of the integrity and initiative in a large body of our citizens? Will our civilization now go down to collapse? It is difficult to conceive this ending, but history is calling loudly upon us to heed the lessons unfolded through succeeding civilizations in the past.

Today, we recognize more than ever before, the equality of man in the community of life—in his physical relations. But we can never have equality of intellectual power in man, nor of spiritual power. We can never have equality of nobility, nor of unselfishness. The most influential will lead; but the most influential are not necessarily, and are not at all times, the most noble and most unselfish. They may be powerful by support of mass numbers with mass psychology, or because of inertia in the most noble and unselfish; and just in the degree of lack of that nobility and unselfishness in those most powerful is there the corresponding likelihood that they will

muster collective action for conflict and the disruption of moral forces for good. There is much consolation and much sound doctrine in the records of human thinking. May we read and study these, that we may develop a philosophy to guide us aright through this convulsive period in world history. Some of this sound doctrine has aroused action, but much has remained unheeded because the impulse for motivation has not taken form.

In the meantime, through all this upheaval, there is gradual shifting over from the shoulders of our profession to the public where it rightfully belongs, all that increasingly heavy burden existing in the economic problem of supplying the costs of our services to the public. We must be careful to guide aright this changing movement, to retain for ourselves the full administration of our scientific advances and their adaptation to the prevention and cure of disease. Let us remain the masters of our services, the servants of the masses under our own noble leadership; not the servants of the State under State leadership.

If we as a profession are to remain true to our traditions—the most noble, the most unselfish, the most influential, we must give noble leadership. Unless we speak with one voice we cannot lead. Unless we have a forum in which the Provincial Medical Associations can come together and determine a single course of procedure we cannot speak with one voice.

The ideal structure for our National Medical Body, the Canadian Medical Association, seems to me to be best described in the words of a judgment handed down by the Imperial Privy Council in 1892. I will read it, substituting for the word "government" the words "Medical Association", as follows: The object is "neither to weld the Provincial Medical Associations into one, nor to subordinate Provincial Medical Associations to a central authority, but to create a Federal Medical Association in which they should all be represented, entrusted with the exclusive administration of affairs in which they have a common interest, each Provincial Medical Association retaining its independence and autonomy."

The goal of the medical profession is the same today as in the day of Dr. Charles Tupper, the same large share in the community life. We have the same mutually accepted objectives; but the method of approach to our goal is rapidly changing. Seventy years ago the approach was largely by the physician alone, in individual contact with his patients; usually dealing with some specific subject at a time of urgent need. Today our approach must overcome much more powerful and ever changing obstructions on the way. It must be by united action on our part for mass education of the public to the nobility of building the highest type of mind and body in our citizens, for recognition of the proper relationship of our profession to the public, and for the solution of any problems tending to disturb that relationship.

May we muster in our profession united action for cooperation, with coordination of effort toward our mutually accepted objectives. Cooperation requires not the acceptance by all of any one or another conception of the means to our ends; it requires not the surrender of any honest convictions; not capitulation to the viewpoints of others, but it does require tolerance of the views of others in seeking to enlarge the field wherein joint effort may function effectively for the realization of our common aims. Only by this joint effort can we do our full part in moving the life of the nation forward; only in this way can we retain our leadership; only in this way can we remain true to our tradition "the most noble, the most unselfish, the most influential of any secular profession or calling."

Hospital Service Department Notes

A New List of Canadian Hospitals Approved for Internship Issued

The 1938 revision of the list of hospitals in Canada which are approved for internship has been issued by the Department of Hospital Service of the Canadian Medical Association. Since the publication of the 1937 list six additional hospitals have been added to the "approved" list and one demoted, bringing the number up to 49 hospitals, furnishing 727 internships. Of these 168 are final year internships under university supervision, the remainder being graduate internships.

The following hospitals have been added to the "approved" list: Mount Sinai Hospital, Toronto; St. Joseph's Hospital, Hamilton; McKellar General Hospital, Fort William; Misericordia Hospital, Winnipeg; Grey Nuns' Hospital, Regina; St. Joseph's Hospital, Victoria.

As in previous issues, a list of "recommended" hospitals is appended. These are hospitals which can provide their interns with an excellent training, but which, for one reason or another, do not comply with the provisions of the basis of approval. Some of these have less than the minimum average daily census of 75 patients; some are highly specialized, so can offer but a limited service; two are beneath the required percentage of autopsies; in some the medical staff is not organized as required by the Basis of Approval.

The arrangement still prevails whereby Canadian students desiring to practise in the United States, or American students desirous of taking an internship in Canada, may obtain credit for their Canadian internship with the National Board of Medical Examiners of the United States. This National Board of Medical Examiners and an increasing number of the states are requiring the completion of a satisfactory internship before certifying as qualified to practise.

Credit is allowed by the United States authorities only for a completed internship in a Canadian hospital approved for internship.

In the last two years it has been noted that an increasing number of students of the graduating classes from unapproved or unrecognized medical schools are endeavouring to find internships in Canada. This coincides with the tightening up by the American Medical Association on the employment of graduates of such schools by hospitals in the United States. No hospital is retained on the "approved" list which accepts graduates of an unrecognized or unapproved school, and the result has been the endeavour

on the part of such students to obtain positions in Canadian hospitals. Were they accepted under the present reciprocal arrangements, such would automatically give them credit for their state board or their examinations. A number of applications have been received from senior students of the Chicago Medical School, which is unapproved, and from the Middlesex College of Medicine and Surgery, of Waltham, Mass., which appears on the "unrecognized" list of the Council on Medical Education and Hospitals of the American Medical Association. All hospitals approved for internship have agreed not to accept interns from unapproved or unrecognized medical schools.

The incidence of autopsies has been included in this year's published list. Since the first list was prepared seven years ago, the rise in autopsies has been most encouraging, and reflects upon the increasing scientific interest of the medical staffs. Many hospitals which a few years ago did only occasional autopsies are now up to 30 and 40 and even 50 per cent of all deaths public and private. Many medical staff members who formerly only sought autopsies on public ward patients have found that they are just as easy to obtain and are just as valuable when done on private patients.

Highest honours go to the Children's Memorial Hospital, of Montreal, which turned in the fine record for the year 1937 of 90.8 per cent! Second place was almost a camera finish, the Montreal Children's Hospital reported 80.8 per cent, and the Montreal General Hospital reported 80.1 per cent. The Montreal Children's Hospital is on the "recommended" list rather than "approved" list, but only because it is not large enough in size to meet the minimum requirements for approval. Fourth position goes to the Jewish General Hospital, of Montreal, with 64.2 per cent. The Hospital for Sick Children, Toronto, comes fifth with 63.1 per cent; the Hôpital Ste. Justine, of Montreal, is sixth with 62.6 per cent; the Women's General, also of Montreal, with 59.8 per cent is seventh. Eighth position was a tie between the Vancouver General Hospital and the Hôpital Notre Dame, of Montreal, with 59.2 per cent. The University of Alberta in Edmonton reported 57.6 per cent for tenth position and the eleventh position went to the Toronto General Hospital with 54.4 per cent. The Hôtel-Dieu of St. Joseph, Montreal, was twelfth with 54.2 per cent. The Children's Hospital, of Winnipeg, was next with 53.2 per cent; Regina General Hospital (52.1 per cent); Royal Victoria Hospital, of Montreal (50.8 per cent), and the Winnipeg General Hospital with 50.2 per cent all exceeded the 50 per cent mark, the Christie Street Hospital, Toronto, having exactly 50 per cent.

It is worthy of note that the Montreal hospitals hold the first four places and seven of the first eight. Two of this group above 50 per cent have surmounted what are usually con-

sidered as real handicaps. The staff of the Jewish General Hospital, of Montreal, has had to overcome considerable racial antipathy to post-mortem examinations, and the Vancouver General Hospital, which is Canada's largest hospital, is a non-teaching institute and only partially closed. The Regina General Hospital deserves similar credit.

Medical Societies

The Fiftieth Anniversary of the American Association of Anatomists

In the Cathedral of Learning of the University of Pittsburgh, and in the palatial Mellon Institute, on April 14th to 16th, the fifty-fourth meeting of the American Association of Anatomists was held, which marked its fiftieth anniversary. President Roosevelt sent personal congratulations. Dr. John Beattie, Conservator of the Museum of the Royal College of Surgeons of England, and Director of Research, came and spoke felicitously for the Anatomical Society of Great Britain and Ireland. Secretary von Eggeling, of the German Anatomical Society, sent official greetings, and other anatomical organizations sent appropriate messages. Among those at the head table at the annual dinner was Professor James Playfair McMurich, of the University of Toronto, one of the oldest members, who was present at the second session of the Association, and who later served as President. He spoke feelingly of the early days of the Association, and of the first President, Dr. Leidy. At the meeting a handsome commemorative medal of Leidy was distributed, done in bronze by the late noted Canadian sculptor, R. Tait McKenzie. It is probably the last work of that great artist. The Association is now the largest of the national anatomical societies, having more than 600 members. A number of Canadian anatomists were present, some of whom took part in the program, which was of great size and varied character. Professor R. R. Bensley, graduate of Toronto, and a pupil of the late A. B. Macallum, gave a paper at the opening session on a new extract of protoplasm called "plasmotin". Secretary Corner retired after eight years of distinguished service, and was replaced fittingly by Professor Eliot Clark. The meetings were presided over by President Frederic Lewis, of Harvard. The new President is Professor S. W. Ranson. A full report will be found in "*Science*" for June 10, 1938.

C. C. MACKLIN

The Canadian Medical Association— Alberta Division

The annual meeting of the Canadian Medical Association, Alberta Division, will be held in Calgary, on September 12, 13 and 14, 1938. The program will include a galaxy of well known speakers from the east and west and from the United States. The list includes Dr. A. T. Bazin, of Montreal, Dr. K. A. MacKenzie, President of the Canadian Medical Association, Dr. J. G. Young, and Dr. T. C. Routley, of Toronto, and Dr. C. Hunter of Winnipeg, representing the Canadian Medical Association, Dr. M. S. Henderson, of the Mayo Clinic, Dr. C. Newburg, of Ann Arbor, Michigan, Dr. R. Coulter, of Northwestern University, Chicago, and Dr. H. Spohn, of Vancouver, will be among the prominent speakers, at what promises to be one of our most successful meetings.

G. E. LEARMONTH

The Canadian Physiological Society

The Canadian Physiological Society held its fourth annual meeting at McGill University, Montreal, on May 23rd. There was an attendance of one hundred and twenty-five. Business and scientific sessions were held in the morning and afternoon. The annual dinner was held in the Windsor Hotel in the evening, when Professor G. F. Marrian addressed the Society on the subject "Speculations upon the metabolism of the steroid hormones".

The Council for 1938-39 was elected as follows:—*President*, Prof. F. R. Miller, University of Western Ontario; *Secretary*, Prof. G. H. Ettinger, Queen's University; *Treasurer*, Prof. E. M. Watson, University of Western Ontario. *Councillors*, Prof. A. Barbeau, Université de Montreal; Dr. J. S. L. Browne, McGill University; Prof. A. T. Cameron, University of Manitoba; Prof. N. B. Taylor, University of Toronto; Prof. D. L. Thomson, McGill University; Prof. E. G. Young, Dalhousie University.

Eleven new members were elected, making a total membership of two hundred and thirty. The Secretary reported that arrangements had been made with the International Physiological Congress Committee by which nineteen communications from Canadian Laboratories are to be presented at the International Physiological Congress in Zürich, August, 1938.

A resolution was passed offering to the Associated Committee on Medical Research of the National Research Council the services and co-operation of the Society in any project, including the publication of a journal. It was decided to hold the next meeting in Kingston, in the autumn of 1939.

Twenty-six communications were presented. Abstracts of some of these are given below.

EFFECT OF AUTONOMIC NERVE STIMULATION AND PRESSOR DRUGS ON THE CARDIOVASCULAR SYSTEM OF ADRENALECTOMIZED DOGS.—R. A. Cleghorn and (by invitation) D. C. Austen, Department of Medicine, University of Toronto.

In acute adrenal insufficiency in dogs there is a marked impairment of the response of the cardiovascular system to splanchnic nerve stimulation and to pressor drugs, with the exception of adrenalin which still exerts a powerful effect (Armstrong, Cleghorn and McVicar, 1937). In chronic insufficiency the cardiovascular system is even more refractory to these drugs, including adrenalin. Adrenalectomized salt-maintained dogs showing normal blood electrolyte values also exhibit abnormal responses to these pressor influences. In addition, they appear to be quite refractory to vagal stimulation.

FURTHER STUDIES OF THE ACTION OF 1, 2, 5, 6-DIBENZANTHRACENE AND PHENANTHRENE CHOLEIC ACID COMPOUNDS IN TISSUE CULTURE.—E. Marie Hearne Creech, Department of Medical Research, Banting Institute, University of Toronto.

An adequate number of cultures of embryonic mouse fibroblasts have been treated with 1, 2, 5, 6-dibenzanthracene choleic acid under carefully controlled conditions. The outgrowth measured on successive days showed a significant increase over the untreated controls and the controls with the non-carcinogenic substance phenanthrene choleic acid.

EFFECT OF GLUCOSE ON GASTRIC SECRETION.—M. H. F. Friedman, Department of Physiology, McGill University, Montreal.

The effect produced on gastric secretion by administration of glucose solutions of various concentrations was studied in dogs and cats. Gastric secretion was stimulated by means of histamine, alcohol or sham-feeding. Glucose solutions were administered intravenously or were introduced into the stomach by mouth or by fistula. It was found that if glucose be given by mouth before the injection of histamine the copious secretion of gastric juice usually obtained by histamine administration is diminished in volume but the concentration of pepsin is not altered. The longer the interval between the giving of glucose and the injection of histamine, the smaller is the inhibitory effect of the glucose. Alcohol in dilute solution when introduced into the gastro-intestinal tract evokes a copious flow of gastric secretion of high acidity but relatively low peptic power. Administration of glucose before the alcohol diminishes the volume of secretion but greatly increases both the concentration and the total output of pepsin. Glucose apparently has a specific trophic effect on the secretion of gastric juice stimulated by alcohol but not on that stimulated by histamine. Gastric juice secreted in response to sham-feeding is very rich in pepsin. Intravenous administration of glucose may lower the volume of the secretion obtained on sham-feeding, but does not increase the concentration of pepsin in the juice, since apparently the peptic cells are already working at their maximum capacity.

INFLUENCE OF METRAZOL AND INSULIN SHOCK TREATMENT (AS USED IN SCHIZOPHRENIA) ON BLOOD FLOW.—B. Leibel (by invitation) and G. E. Hall, Department of Medical Research, Banting Institute, University of Toronto.

Insulin shock produces an initial rise in blood flow from the jugular vein of over 50 per cent, the simultaneous record from the carotid remaining normal. Following the initial venous increase the carotid and jugular

blood flows then simultaneously decrease slowly to normal. Metrazol shock produces an initial increase in carotid blood flow of about 40 per cent. With the onset of coma the carotid flow then decreases some 200 per cent. After 10 to 12 minutes the flow returns to normal and then shows a periodic fluctuation for over one hour.

AN EFFECT OF ASCORBIC ACID UPON THE WEIGHTS OF GUINEA PIGS.—E. W. McHenry, and (by invitation) E. J. Reedman and Margaret Sheppard, School of Hygiene, University of Toronto.

Anorexia has been regarded as a characteristic symptom of a deficiency of vitamin B₁. However, a deficiency of ascorbic acid causes a loss in appetite with a subsequent loss in body-weight in guinea pigs. Since anorexia is likely also to be found in other vitamin deficiencies it should no longer be regarded as specifically associated with a lack of vitamin B₁. In paired feeding experiments animals receiving a scorbutic diet plus ascorbic acid are significantly heavier than animals, of the same initial weight, receiving only the basal diet. The difference in weight cannot be due to difference in food intake and is believed to be caused by alterations in metabolism induced by ascorbic acid. These results offer a promising lead for an investigation of the physiological function of ascorbic acid.

INTESTINAL LESIONS PRODUCED BY HISTAMINE IN THE RAT.—Hans Selye, Department of Anatomy, Histology and Embryology, McGill University, Montreal.

Previous experiments have shown that a single intravenous injection of 50 mg. of histamine may elicit an acute phlegmonous inflammation of the cæcum in the rat (Selye, Hans, *The Lancet*, 1936, p. 1210; *The Canadian Medical Association Journal*, 1937, 36: 141). In recent experiments, three daily injections of 10 mg. of histamine were given subcutaneously for a period of 21 days to rats weighing 80 to 100 g. At the end of this time all these animals developed severe diarrhœa and a histological study of their intestinal tract showed inflammatory lesions with marked round-cell infiltration, not only in the cæcum but also in the small and large intestine. These experiments offer further evidence showing that histamine has a specific effect on the alimentary tract, even in animals such as the rat, which are known to be extremely resistant to this substance. Since recent experiments made it very probable that histamine is discharged from tissues under the influence of noxious agents it seems possible that various intestinal lesions of hitherto cryptic etiology may be due to an endogenous intoxication by histamine or similar metabolites.

THE VITAMIN A AND CAROTENE CONTENT OF COW'S MILK.—A. J. Sutherland (by invitation) and W. D. McFarlane, Macdonald College, McGill University, Montreal.

Information regarding the vitamin A and carotene content of milk produced in Canada under winter conditions of stall-feeding is not available. For a comprehensive survey only chemical or physical methods of determining vitamin A would be practical.

When the colorimetric or spectrophotometric methods now in use are applied to milk several difficulties are encountered. A procedure was finally developed which, it was considered, would give results of at least relative values. A preliminary study indicates that as winter progresses the decrease in the vitamin A content of the milk is relatively small but the carotene content drops about fifty per cent.

In addition, the following papers were read.

PRELIMINARY REPORT ON A CHEMICAL INVESTIGATION OF HUMAN HAIR.—James Beveridge, Jr. (by invitation) and C. C. Lucas.

PLACENTAL ACETYLCHOLINE.—G. H. Ettinger and (by invitation) G. L. Bateman.

A TYNDALLMETER ATTACHMENT FOR THE MEASUREMENT OF TURBIDITY WITH THE PHOTO-ELECTRIC COLORIMETER.—Kenneth A. Evelyn.

MORPHOLOGICAL CHANGES PRODUCED BY THE ALARM REACTION IN THE GUINEA PIG.—Virgilio G. Foglia (by invitation) and Hans Selye.

GLYCOLASE IN B_1 DEFICIENT RATS.—W. R. Franks and (by invitation) A. E. Byrnes and L. D. Proctor.

THE RELATION OF THE VITAMIN B COMPLEX TO FAT METABOLISM.—E. G. Gavin and E. W. McHenry.

A FOUR-CHANNEL AMPLIFYING SYSTEM FOR SIMULTANEOUS RECORDING.—J. E. Goodwin (by invitation).

HEARING IN NORMAL AND HYPOPHYSECTOMIZED RATS.—Rhoda Grant (by invitation) and Simon Dworkin.

FURTHER STUDIES ON THE EFFECT OF THE ALARM REACTION ON WATER EXCRETION.—St. Karády, (by invitation), J. S. L. Browne and H. Selye.

SLOW POTENTIAL WAVES SET UP IN THE INFERIOR MESENTERIC GANGLIA BY PREGANGLIONIC AND ANTIDROMIC VOLLEYS.—D. P. C. Lloyd (by invitation).

THE FATE OF INTRAVENOUSLY INJECTED O_2 AND CO_2 .—D. W. Loughheed (by invitation) and G. E. Hall.

A BIOCHEMICAL INVESTIGATION OF THE THERAPEUTIC USE OF SULPHANILAMIDE.—C. C. Lucas.

STUDIES ON THE DIAZO REACTION OF BILIRUBIN IN SERUM.—Helga Tait Malloy and Kenneth A. Evelyn.

A METHOD FOR THE DETERMINATION OF GLUCURONIC ACID IN AQUEOUS SOLUTION AND IN URINE.—G. B. Maughan (by invitation), J. S. L. Browne and K. Evelyn.

ON THE CHEMISTRY OF α -TOCOPHEROL (VITAMIN E) AND ITS DERIVATIVES.—C. S. McArthur (by invitation) and E. M. Watson.

THE HISTOLOGICAL FEATURES OF THE RESPIRATORY PROTOPLASMIC MEMBRANE BETWEEN BLOOD AND AIR IN THE ADULT MAMMALIAN PULMONIC ALVEOLAR WALL.—Charles C. Macklin.

THE PHYSIOLOGICAL PROPERTIES OF A THERMOSTABLE EXTRACT OF PITUITARY TISSUE.—D. K. O'Donovan, A. H. Neufeld, O. F. Denstedt (by invitation) and J. B. Collip.

THE PHYSIOLOGY OF HAIR STRUCTURE AND PIGMENTATION.—Sheldon C. Reed (by invitation).

THE RELATIVE POTENCY OF VARIOUS LIPOTROPIC FACTORS.—Jessie H. Ridout and C. H. Best.

Abstracts of all papers are included in reprints which may be obtained on application to the Secretary, G. H. Ettinger, Queen's University, Kingston, Ontario.

Nova Scotia Medical Society

Dr. J. H. L. Simpson, of Springhill, was elected *President* of the Medical Society of Nova Scotia (now, the Canadian Medical Association, Nova Scotia Division) at the annual meeting in Halifax in June. He succeeds Dr. Allister Calder, of Glace Bay.

The *Vice-presidents* are Dr. H. K. MacDonald, Halifax; Dr. A. B. Campbell, Bear River; *Secretary*, Dr. H. G. Grant, Halifax; *Treasurer*, Dr. W. L. Muir, Halifax.

The Association decided to hold its next annual meeting at Digby. Visiting delegates introduced were Sir Humphry Rolleston, of Surrey, England, of the British Medical Association, and Dr. Bowman Crowell, Chicago, of the American College of Surgeons.

The annual meeting of the Nova Scotia Medical Society was held in June in conjunction with the Canadian Medical Association convention. Naturally subservient to the greater event, business sessions were cut to a minimum and no new business of an outstanding nature was introduced. Reports of the various committees were presented and adopted, most important of these being the finalizing report recommending affiliation of the provincial society with the Canadian Medical Association. Dr. J. H. L. Simpson, of Spring Hill, was elected president for the ensuing year, Dr. H. G. Grant and Dr. Walter Muir continuing as secretary and treasurer, respectively.

The Regina General Hospital

At the annual meeting of the Medical Staff of the Regina General Hospital the following officers were elected: *Past-President*, Dr. B. C. Leech; *President*, Dr. C. R. May; *Vice-president*, Dr. F. D. Munroe; *Secretary-treasurer*, Dr. John Farr; *Executive Committee*, Drs. O. E. Rothwell, D. C. MacRae and D. W. Johnstone; head of medical services, Dr. A. C. MacMillan; and head of surgical services, Dr. D. S. Johnstone.

The surgical committee has recommended that a board of five consultants be appointed to act without remuneration when a consultation is necessary in cases of sterilization and abortion. The board of consultants appointed by the Board of Governors is as follows: Drs. W. A. Thomson, R. McAllister, W. A. Harvie, F. J. Ellis, and H. L. Jackes. Their duties are to commence as from July 1, 1938. Appointments are for one year. When the operation of sterilization and abortion is requested to be done it will be necessary to have one or more of these consultants pass on the case before the contemplated operation may be proceeded with.

LILLIAN A. CHASE

The Saskatoon City Hospital Staff

A meeting of the Saskatoon City Hospital Medical Staff was held on May 20th. Dr. J. A. Valens reported a case previously reviewed two months ago. Typhoid agglutination was present, but a non-haemolytic streptococcus was isolated from the blood. In the meantime the patient had been examined at the Mayo Clinic and returned to Saskatoon with diagnosis confirmed, namely, subacute bacterial endocarditis; they also confirmed the grave prognosis. Dr. C. Kirk presented an interesting cutaneous lesion in a man who had a red dermatitis on the neck, hands and back, with oedema of legs and ankles. No diagnosis was arrived at. The case will be presented for further review. Dr. L. Schulman reported a case, a woman aged 44, who had had resection of colon for carcinoma in 1934. Three and a half years afterwards she had sudden onset of cerebral symptoms of

unlocalized brain tumour. Post-mortem examination showed a large metastatic carcinoma in the anterior lobe.

At the June meeting of the same Society Dr. B. R. Burwash spoke on anæsthesia. He said that the proper term for "spinal anæsthesia" is "spinal analgesia". The dangers of this form of anæsthesia are paralysis of the sympathetic supply of the heart and paralysis of the respiration. He gave an outline of the technique. Injection should be done slowly. The contraindications are cardiac deficiency, septicæmia, and neurosis. Some indications are the presence of jaundice and alcoholism. The post-operative sequelæ are headache, ileus, and bladder atony. Dr. L. H. McConnell in discussion said that spinal anæsthesia was of no value in operations on the cord, and that post-operative headache was probably due to leakage of spinal fluid.

A letter of sympathy was sent to Dr. E. E. Shepley, radiologist, who has resigned on account of ill health.

LILLIAN A. CHASE

The Tri-County Medical Society

A very successful and highly instructive meeting was held in the Medical School of the University of Western Ontario, London, on June 8th, when three neighbouring Medical Societies—Middlesex, St. Thomas and London, joined in a symposium on "Gastric and duodenal ulcerations". The divisions for consideration follow.—(1) the problem of dyspepsia in general practice—Dr. H. Fletcher, Arva; (2) review of physiology, anatomy and laboratory methods—Dr. Fred Luney, London; (3) clinical symptoms and medical therapeutics—Dr. J. H. Geddes, London; (4) radiological diagnosis—Dr. A. W. McPherson, St. Thomas; (5) surgical indications—Dr. R. Bristow, St. Thomas. The discussion and summary were taken by Dr. E. E. Cleaver, of Toronto and Dr. S. Houston, of Kingston.

A pathological exhibit was contributed by Dr. J. Fisher, of the University, and a joint radiological exhibit was presented by Dr. M. Morrison, London, and Dr. R. A. McPherson, St. Thomas.

A supper followed the meeting and at its close a "Question Box" discussion was active, and culminated a very instructive meeting. Drs. Cleaver, Fisher, Watson, Morrison, Carrie and Geddes having the duty of adding the last word of counsel.

From an observer's standpoint it may be said of this innovation that advantage is evident in (a) making an exhaustive study of one subject at one meeting; (b) developing the idea that the general practitioner and the specialist can combine efforts to mutual advantage; (c) co-ordinating the membership of adjacent societies in a joint meeting in the spirit of good neighbours.

GEORGE A. RAMSAY

The Western Nova Scotia Medical Society

The Western Nova Scotia Medical Society, in annual meeting, elected as *President*, Dr. G. Victor Burton; *Vice-presidents*, Drs. H. H. Banks, E. A. Ferguson and E. L. Eagles; *Secretary-treasurer*, Dr. T. A. Lebbetter. Dr. A. B. Campbell, retiring president, was in the chair.

Post-Graduate Courses

University of Toronto

POST-GRADUATE COURSE ON METABOLIC AND ENDOCRINE DISORDERS

The University of Toronto, Faculty of Medicine, offers to graduates in medicine a course of one week, September 19th to 24th, inclusive. This course will consist of theatre and bedside clinics and practical work in the wards of the Toronto General Hospital. It will be limited to twenty and will be given only if at least ten practitioners signify their intention of attending.

Applications will be received up to August 15, 1938. Write to the Secretary, Faculty of Medicine, University of Toronto, at whose office registration will take place.

A fee of \$25.00 will be charged.

POST-GRADUATE COURSE ON CANCER

The University of Toronto, Faculty of Medicine, offers to graduates in medicine who are particularly interested in surgery and radiotherapy a course of one week on cancer commencing Monday, October 3rd.

This course will consist of lectures, clinics, surgical operations and demonstrations in radiotherapy and will be conducted by the departments of surgery, gynaecology, otolaryngology, radiology and pathology.

The course will be limited to twenty students.

Applications will be received up to September 15th. Write to the Secretary, Faculty of Medicine, University of Toronto, at whose office registration will take place.

A fee of \$25.00 will be charged.

Information for Doctors in Berlin

There has been set up in the Kaiserin Friedrich-Haus, Berlin N W 7, Robert Koch-Platz 7, a bureau which will be able to give doctors every kind of information. The office is semi-official, and gives advice impartially and free of charge. It would be to the advantage of every doctor to get into touch before or after his arrival in Berlin with the Kaiserin Friedrich-Haus, so as to save time and make the most of his stay.

Medico-Legal

Diversion of Gift from American to English Hospitals

A very unusual case has been closed recently in the British High Court of Justice. Five years ago a London bachelor died, leaving an estate of some \$900,000. After making bequests which left a number of relatives disinherited, the residue, amounting to approximately \$500,000 after payment of succession duties, was left for the use of hospitals and other charities. Originally English hospitals were specified, but shortly before his death he became involved in a dispute with the London County Council which wished to obtain his home estate for an extension of Maudsley Hospital. Not being able to gain possession otherwise, the Council obtained parliamentary authority to condemn his property. Angered at this action, the owner then attached a codicil to his will directing that the net proceeds go to hospitals and charities in the United States instead of in England.

After his death some of the disinherited relatives living in Germany contested the will and attempted to prove that the testator was not of sound mind. Because of international difficulties the final decision was considerably delayed but has now been given. It has been held by the Court that the testator was of sound mind in cutting off most of his relatives and in giving the funds to the hospitals and other charities to be selected by his executors. But the Court ruled that the codicil which would send the money to the United States was dictated by the testator's insane delusion concerning the London County Council. It was directed, therefore, that the funds be used for hospitals in England as though the 1932 codicil had never been written.

Topics of Current Interest

Benzedrine Sulphate — A Warning

Following the appearance of items in the press during the last few weeks many inquiries have been received concerning the use of benzedrine sulphate in the treatment of obesity. Sensational reports on the effects of benzedrine sulphate are not new to the medical press or to the daily newspapers. Some months ago the Journal published a critical editorial on benzedrine sulphate.¹ At that time the drug was being used unwisely to avoid fatigue; news that it could be obtained for keeping one awake while "cramming" for final examinations spread from campus to campus. The drug has been employed for such widely variable con-

ditions as anginal pain, seasickness and apathy. Now it is suggested for weight reduction. While not as toxic as the ill-famed reducing agent dinitrophenol,² nevertheless its use may be followed by serious consequences. Just as the Council on Pharmacy and Chemistry issued a report on the status of dinitrophenol, it has recently published a report on benzedrine sulphate.³ The Council concluded that in the light of available evidence claims for benzedrine sulphate should be limited to its usefulness in narcolepsy, postencephalitic parkinsonism and certain depressive mental states encountered in institutionalized patients. In this report it was noted that Nathanson had described a loss of appetite following the use of the drug for the avoidance of fatigue; hence it seemed to be potentially a drug which would be somewhat effective in obesity.

The recent publicity is based on the latest report by Myerson and his associates⁴ in the Division of Psychiatric Research at the Boston State Hospital. The use of the drug in obesity is advocated on the premise that in many cases this condition is associated with anhedonia (defined by Myerson as "a diminution, even to the point of disappearance, of satisfactions normally obtained from life activities, and in loss or distortion of appetites and desires"). Myerson believes that these patients have a tendency to eat too much and too often, to nibble between meals, not only in an attempt to satisfy the appetite but to escape from their neurosis. Proceeding on this basis, Myerson and his associates employed a 1,400 calorie diet and gave the patients benzedrine sulphate for the purpose of making them satisfied with this calorie intake; reductions were reported, averaging a pound a week. Myerson's work with this drug has been extensive, yielding much clinical evidence concerning its effects. It must be remembered that when Myerson recommends the drug for certain purposes, he frequently refers to its use in conditions as they occur in patients coming under the purview of the psychiatrist and neurologist. It does not necessarily follow that such results may be safely or effectively produced in otherwise normal persons. The Council in recognizing the usefulness of benzedrine sulphate in the treatment of narcolepsy decries its use for sleepiness and fatigue in those who are otherwise normal. Many of Myerson's cases concerned definitely psychoneurotic patients

1. Benzedrine sulphate "Pep Pills", editorial, *J. Am. M. Ass.*, 1937, 108: 1973.

2. Dinitrophenol not acceptable for N. N. R., report of the Council on Pharmacy and Chemistry, *J. Am. M. Ass.*, 1935, 105: 31; Dangers of slimming, current comment, *ibid.*, 1935, 105: 804.

3. The present status of benzedrine sulphate, report of the Council on Pharmacy and Chemistry, *J. Am. M. Ass.*, 1937, 109: 2064.

4. MYERSON, ABRAHAM, AND LESSES, M. F.: Human autonomic pharmacology: XVI. Benzedrine sulphate as an aid in the treatment of obesity, *New Eng. J. Med.*, 1938, 218: 119.

classed as suffering from anhedonia. He treated the obesity by reducing the caloric intake, and the anhedonia by administering benzedrine sulphate. It may be assumed, therefore, that the drug might fail to reduce weight effectively in the normal person who does not suffer from anhedonia.

Myerson's report gave the details of eight of a total of seventeen cases. The diagnosis of three of these was "obesity with psychoneurosis". Other diagnoses were "obesity with hypermenorrhœa," "obesity following subtotal thyroidectomy," "obesity—failure of benzedrine to aid in reducing weight" and just plain "obesity".

Benzedrine sulphate is contraindicated in many conditions, especially in cardiac conditions, which are not infrequently seen in the obese. Finally, evidence is accumulating which indicates that its use may produce craving and even addiction in some instances.

Both the Journal and the Council have previously noted that this drug is too new to pharmacology and experimental medicine to warrant any prediction as to the possible harm that may result from its long continued use. Even if benzedrine sulphate could be safely and effectively used to reduce weight there is no evidence that it will have any permanent effect on weight. Its use over long periods is certainly not without danger, particularly to the circulatory system. Physicians may well warn patients against the indiscriminate use of the preparation to control obesity. Benzedrine and its sulphate are promising drugs when used properly.—*J. Am. M. Ass.*, 1938, 110: 901.

Freshmen Grow in Stature

As there has been considerable discussion about the stature of university students during the past few years, it may be of interest to compare the figures of the University of Toronto students with those of some of the leading American universities. From these it will be seen that our students stand first in height and second in weight, thus tying with Harvard for first place in general average.

The following table of figures shows the

COMPARATIVE STATISTICS ON STATURE OF FRESHMEN*

University	Height Inches	University	Weight Pounds
Toronto	69.88	Harvard	148.2
Harvard	69.5	Toronto	144.51
Princeton	69.28	Stanford	144.36
Yale	69.24	Yale	143.52
Stanford	69.21	California	142.58
California	69.05	Texas	142.36
Texas	69.01	Wisconsin	141.94
Minnesota	68.56	Princeton	141.55
Cincinnati	68.55	Minnesota	140.66
Cornell	68.48	Cornell	139.93
Wisconsin	68.25	Coll City, N.Y.	139.42
Coll City, N.Y.	67.02	Cincinnati	138.64

* (This table of figures, apart from those of Harvard and Toronto, is taken from Diehl's textbook on "Healthful Living".)

height and weight of the average freshmen in twelve universities.

That the general average is increasing is shown by the following figures:

Among 665 Harvard freshmen, average age 18 years, the gain in height during the past 15 years is $1\frac{1}{2}$ inches, and in weight 5.2 pounds.

Among the 820 Toronto freshmen (1937-38), average age $18\frac{1}{2}$ years, the gain in height compared with the freshmen of 1921-22 is $1\frac{3}{4}$ inches, and in weight $7\frac{1}{2}$ pounds. In this year's class of freshmen, there are 152 who are six feet tall or over, with an average weight of 159 pounds. Approximately every sixth freshman this year is six feet tall or over. The average gain in weight of our students during his first year is three pounds.

In an article appearing in the British Anthropological Journal, *Man* (August, 1937) on "Some observations concerning the stature of freshmen entering the University of Toronto", John Allan says that "The general trend of height and weight standards is still observable after the depression years", and he is inclined to believe that "this increase is due in part to improved knowledge of dietetic principles, and their application in practice".

In comparing our students with those in England, he says that, "The average height of English Public School boys of eighteen is almost exactly the same as that for freshmen of the same age in Toronto. In this connection it should be remembered that those entering the University in Canada in general come from less wealthy homes than do the English group referred to".

It may be of interest to add that according to the Metropolitan Life Insurance Company, which has made a special study of mortality among very tall men, they say that "It was found that as a group these men had a practically normal mortality", and that "The prospective longevity of this growing contingent in our population need cause us no concern".—George D. Porter, Director of University Health Service. From the *University of Toronto Monthly*, December, 1937.

Mosquito Bites

Some years ago the Medical Officer of Health for Belfast advised oil of lavender on the hair or clothes as a preventive of mosquito bites. "As the mosquito frequently bites about the ankles, two pairs of thin socks or stockings are better than one thick pair. . . . To protect the face use a 50 per cent alcoholic solution of thymol, or oil of cloves in lanoline. If bitten, dab on at once a weak solution of ammonia or of washing soda or common soap and vinegar, or apply a cut onion to the sore. If the irritation is severe apply iodine in glycerin."—From *Brit. M. J.*

Abstracts from Current Literature

Medicine

Experimental Studies on the Effect of Temporary Occlusion of Coronary Arteries. Blumgart, L. *et al.*: *Am. J. M. Sc.*, 1937, 194: 493.

Heberden's angina pectoris is due to temporary ischæmia, while coronary occlusion is the result of permanent ischæmia with infarction.

This is a study in search of a change in the electrocardiogram or anatomy when the blood supply is temporarily cut off. The anterior descending coronary artery of 24 cats was occluded for from five to forty minutes and the traction subsequently released, and most of the animals allowed to survive one to nine days. Electrocardiography was done at various intervals during and following occlusion and showed anoxæmic changes in the post-operative days of all animals in which occlusion was done, for from fifteen to forty minutes inclusive. Only three of the six cats in which the occlusion was less than ten minutes showed post-operative change. These changes persisted in one animal until its sacrifice eight days after operation. The electrocardiographic changes were of the anterior infarction type. Autopsy failed to show gross or histological evidence of cardiac infarction in any case. At times during occlusion, but particularly after release, ventricular extra systoles and ventricular fibrillation developed. Three of the five cats with the latter irregularity died immediately. One of the cats fibrillated on release of the ligature but recovered. When the occlusion of the anterior coronary artery exceeded fifteen minutes the changes consisted in (1) elevation or depression of the S-T take off; (2) loss of the S-T segment, and (3) change of the direction, amplitude and contour of the T wave. In most of the animals these electrocardiographic changes occurred within one minute of occlusion of the vessel, increased during the first post-operative day, and slowly subsided.

Counterparts of these experimental findings are seen in patients with angina pectoris. Electrocardiograms during attacks are characteristic of myocardial ischæmia, but revert to normal at the end of the seizure. Many angina patients show persistent electrocardiographic abnormalities without post-mortem evidence of coronary occlusion or myocardial infarction. The pathological changes produced seemed to fit into an intermediate zone between the two extremes, where myocardial damage had been stopped just short of causing gross tissue destruction, yet functional mischief was so profound that electrical recovery was incomplete for periods as long as nine days. Special technique might have shown changes in staining reactions and metabolism.

The frequent occurrence of ventricular fibrillation in these experiments is in accord with the view that sudden death in angina pectoris is due to the onset of this arrhythmia.

C. R. BOURNE

Syphilis of the Interventricular Septum and Ventricular Tachycardia. Cossio, P. *et al.*: *Am. J. M. Sc.*, 1937, 194: 369.

The rarity of syphilis of the myocardium makes this case interesting. The author states that he can find no other similar report of proved syphilis of the interventricular septum with ventricular tachycardia in the literature. The report refers to a sailor, aged 35, admitted to the British hospital in Buenos Ayres in prostration which began 10 days earlier on board ship. The electrocardiogram showed ventricular tachycardia. The patient died suddenly during an attack of coughing and dyspnoea. Autopsy showed a lesion of the sclero-gummatous type with endo-coronaritis and *Treponema pallidum* (Darier's microscopic gumma) was found in it. An illustration shows a microphotograph of the myocardial mononuclear infiltration as well as the treponema. The electrocardiogram taken shortly before death is shown illustrating the ventricular tachycardia not unlike auricular flutter.

The writer is of the opinion that "in a case of prolonged attack of ventricular tachycardia, provided that the Wassermann and Kahn tests are positive, we must not only suspect infarction of the septum of the ordinary type but also of syphilitic etiology".

C. R. BOURNE

Metabolism of Vitamin "C" in Rheumatoid Arthritis. Rhinehart, J. F., Greenberg, L. D., Baker, F., Methier, S. R., Bruckman, F. and Choy, F.: *Arch. Int. Med.*, 1938, 61: 537.

Following previous observations on changes in articular tissues in chronic scurvy the authors investigated the question clinically. One point to be decided was whether it was vitamin C deficiency from poor absorption. A common finding in scurvy and many cases of arthritis is spongy gums which suggests a lowered capillary strength, also that similar tissue changes in joints would predispose to granulation tissue formation and succeeding degenerative processes, providing favourable sites for bacterial localization. Since it is now possible to estimate the vitamin C (cevitamic acid) content of the blood accurately, as regards the patients' nutrition in this respect, the authors were able to compare the normal with the deficient types. Normal controls were compared with cases of rheumatoid arthritis and other types of joint involvement; 0.7 to 0.9 mg. per 100 c.c. is considered adequate and below 0.5 mg. a deficiency. Results showed that cases with true rheumatoid arthritis and rheumatoid types of arthritis all gave readings much below normal. A small group of gonor-

rheal arthritis cases also were low. Hypertrophic arthritis cases showed high values. Practically all responded promptly to big doses of vitamin C.

As shown by clinical improvement an occasional patient apparently could not make use of vitamin C and did not respond.

P. M. MACDONNELL

Surgery

Effect of Hypoproteinemia on Wound Disruption. Thompson, W. D., Ravdin, I. S. and Frank, I. L.: *Arch. Surg.*, 1938, 36: 500.

The rupture of abdominal wounds continues to occur in 1 to 3 per cent of all abdominal operations, especially after operations on the upper part of the gastro-intestinal tract or on the biliary tract. The mechanical factors incident to an incision in the upper part of the abdomen, the use of catgut, the tensile strength of which may rapidly decline, and allergic reactions to the suture material are probably not the only factors associated with this complication when local factors pertaining to the wound have been controlled. The authors believe that they have an explanation for disruption of the wound in certain cases and a method of control. This they proved experimentally on the dog, where there was advanced hypoproteinemia following operation and where every other factor but this one, which they could control, had been controlled. Healing of the wound was greatly retarded whether silk or catgut sutures were used, but internal disruption was greater with catgut. The failure of the wound to heal was, they believe, associated with the hypoproteinemic state, a condition which is present in many patients subjected to operations on the gastric, duodenal and biliary tracts.

G. E. LEARMONTH

Malignant Neoplasms of the Nasopharynx. Furstenberg, A. C.: *Surg., Gyn. & Obst.*, 1938, 66: 400.

Neoplasms in this region may be classified into 4 groups, depending upon tissue derivation. The carcinomata develop from the epithelial structures, the sarcoma from connective-tissue elements, the lymphoblastoma from the lymphatic structures, and the teratoma which represents the *Anlage* of any of these three. Lymphatic metastases occur to the upper cervical lymph-nodes, but the most marked feature of these neoplasms is their marked tendency to spread upwards to the base of the cranium. Involvement of the cranial bones frequently occurs early, with the probable course along the lymphatics of the pharyngo-tympenic (Eustachian) tube. Invasion by continuity occurs towards the cranium with early signs of pressure on or paralysis of the cranial nerves as they emerge through their foramina. The early

signs in order of frequency are: (1) cervical swelling, 60 per cent; (2) pain in ear, head and throat, 50 per cent; (3) unilateral deafness, 37.5 per cent; (4) changes in the membrana tympani, 25 per cent; (5) 6th cranial nerve paralysis, 20 per cent; (6) 5th (trigeminal) cranial nerve impairment. The average duration of symptoms before diagnosis in 40 cases was 15 months; yet, the routine examination of these passages with biopsy is usually sufficient to establish the diagnosis. Teratomas, such as "craniopharyngioma", chordomas, adeno-carcinoma arising from columnar epithelium remaining undifferentiated as embryonic tissue are not infrequent. The chordomas are slowly infiltrating lesions with varying degrees of vacuolation. The mortality in this series has been nearly 100 per cent within 2 years of diagnosis, although all recent methods have been used.

FRANK DORRANCE

Two-plane Direction Finder for Nailing Fractures of Neck of Femur. Engel, G. C. and May, H.: *Surg., Gyn. & Obst.*, 1938, 66: 495.

Building upon a clue from Kuentscher's clinic the authors have had two simple planes made which will allow accurate and quick insertion of a Smith-Petersen pin. The technique of application is given in full detail. They were able to complete the insertion in 20 minutes with the two cases upon which they had the opportunity to use the two-plane direction finder. They stress (1) the simplicity; (2) the accuracy of insertion; (3) the small incision; (4) the short duration of operation; (5) the patient is able to be up in a chair in 48 hours, so there is early motion and less chance of atrophy of disuse; (6) accurate measurement of the nail to be used, so that impaction of the fragments can be made without fear of penetration of the acetabulum.

FRANK DORRANCE

Spurs of the Os Calcis. Steindler, A. and Smith, A. R.: *Surg., Gyn. & Obst.*, 1938, 66: 663.

The association of painful heels with spurs is of infrequent occurrence. Avoidance of weight-bearing assures relief. Seventy-one patients were treated conservatively with 44 per cent, that is 31 feet, complete relief during an average time of 10 months; 31 per cent had to have operative measures. The conservative measures used consisted of a felt or solid leather insole with a hole cut over the point of the spur, with occasionally a soft rubber sponge applied over this. In 28 feet a posterior wedge had to be cut in the heel of the shoe to insure relief. This was used in addition to the insole. Twenty-two feet had to be operated upon. Four of these patients chose immediate operation rather than trial of conservative measures. Sixteen had a simple excision of the spur; in 2 of these recurrence took place, so that 8 feet had the

curved osteotomy of the os calcis with the removal of a wedge from the inferior surface of the anterior portion, the tendo Achillis was lengthened, and the spur inserted into the wedged portion of the bone by anterior and superior rotation of the posterior portion of the os calcis. Fixation in that position was made by a steel pin or ivory bone peg. FRANK DORRANCE

Obstetrics and Gynecology

The Problem of Endometriosis. Dougal, D.: *Am. J. Obst. & Gyn.*, 1938, 35: 373.

In the majority of cases the theories of Cullen and Sampson adequately explain the source of origin of the endometrial elements. Trauma and inflammation may be predisposing factors but the exciting cause of the invasive process is probably an excessive secretion of the hormone responsible for endometrial proliferation. The naked eye and microscopic appearances of endometriosis are unmistakable. In the case of the uterus there is a diffuse or nodular thickening of the muscle wall composed of hyperplastic fibromuscular tissue and seams or islets of endometrium. In external endometriosis the earliest manifestation is the presence of a number of minute purplish blood implants on the surface of the pelvic organs and in the anterior and posterior cul-de-sac. The subsequent life history of these implants depends on their proliferative activity and on their situation. The ovary and pouch of Douglas are the most favourable sites for continued growth, and the majority of lesions of clinical importance are to be found in these situations. External endometriosis of the uterus is an almost invariable accompaniment of ovarian and rectovaginal endometriosis. Fibroids are present in more than one-third of the cases of external endometriosis.

Every woman is exposed to the danger of endometriosis during the reproductive period of her life. The lesions which may result are of an infiltrative character and, except in their early stages, are not readily amenable to conservative treatment. Endometriosis seriously interferes with the conservative treatment of uterine fibroids.

For every 100 cases of uterine fibroids there are 6 cases of internal and 25 cases of external endometriosis. The latter is met with as the principal lesion or as an important complication in not less than 10 per cent of all abdominal operations on the female generative organs.

The principal symptoms are abdominal pain, menorrhagia, dysmenorrhœa and dyspareunia. Endometriosis has a serious adverse influence on fertility. When the lesions are extensive Dougal prefers to remove the uterus, preferably by total hysterectomy, together with both appendages. It should be possible to reduce the incidence of external endometriosis by treating subinvolution, backward displacements of the uterus, and uterine fibroids.

Early diagnosis depends on proper appreciation of the importance of such symptoms as acquired or increasing dysmenorrhœa, particularly if associated with menstrual irregularity, pain in the vagina or on defæcation, and high dyspareunia. The earliest of the characteristic physical signs is some diminished mobility or some asymmetry of the uterus. Dysmenorrhœa or dyspareunia of recent origin should always arouse a suspicion of endometriosis, and in the absence of well-marked physical signs be sufficient to warrant a careful examination under anæsthesia or even an exploratory abdominal operation. ROSS MITCHELL

Menstrual Periodicity; Statistical Observations on a Large Number of Normal Cases. Dunn, et al.: *Brit. J. Obst. & Gyn.*, 1937, 44: 839.

Because of such varied opinions on menstrual periodicity and its important relation to fecundity the authors made an extensive review of gynecological histories, and also conducted a campaign through the committee of the Medical Women's Federation, data being obtained in 6,000 school girls. The authors make a study of lunar attractions and neap tides in sexual behaviour of insects, worms, and sea fishes. They also suggest the possibility of lunar rhythm in human menstruation. The authors clearly summarize their extensive investigations by stating that 90 per cent of women had an average interval between 25 and 36 days inclusive. Three per cent had an average of 37 days or over. Two per cent had an average of less than 24 days. The average interval did not show any predilection for whole weeks. The average in all cases was 29 days. No cases were found which did not show at least 2.75 days between the shortest and longest interval. Marriage, seasons of the year, lunar attractions, or status of employment did not alter the interval. Of these 770 cases carefully studied 209 were reliable, 270 fairly reliable, and 291 unreliable.

P. J. KEARNS

Œdema in Pregnancy. Nixon, W. C. W.: *Brit. J. Obst. & Gyn.*, 1938, 45: 48.

The author reviews 2,244 obstetrical deliveries in the clinic of Hong Kong. Of these 16.3 per cent, or 366 cases, had some form of œdema. He mentions many associated causes of œdema, such as heart disease, nephritis, aplastic anæmia, and some causes which are peculiar to the country, such as epidemic dropsy, transient œdema, and the œdema associated with ankylostomiasis. The main symptoms of œdema found in the pre-eclamptic differ from those in other diseases. In the œdema of toxæmia of pregnancy the main symptoms are albuminuria, headache, dimness of vision, epigastric pains, and raised blood pressure. In the treatment of marked œdema the injection of 50 to 100 c.c. of 50 per cent glucose solution intravenously is advocated.

Some cases require vitamin B because there is an inter-relation between vitamin deficiency, the endocrine disturbances and the condition of toxæmia of pregnancy. The weight of the patient is the best test for a decrease or increase of œdema. With the onset of œdema very little change in blood pressure was noted, but in the latter cases there was a gradual rise in blood pressure.

P. J. KEARNS

Fibroma of the Ovary: A Clinical Study.

McIlrath, M. B.: *Brit. J. Obst. & Gyn.*, 1937, 44: 1102.

The occurrence of fibroma of the ovary is from 2.25 to 5.9 per cent of all ovarian tumours. According to various authors the majority of these tumours were removed from parous women near the menopause. Pelvic pain, dysmenorrhœa, and metrorrhagia were frequent symptoms of distress. Abdominal swelling and pressure symptoms in the abdomen and rectum were also present. The majority of patients had a history dating over one year. Left-sided tumours were more frequent than right; bilateral tumours were rare. The presence of fibroma of the ovary associated with pregnancy is also rare.

P. J. KEARNS

Therapeutics

Wheat Germ Oil Therapy. Shute, E.: *Am. J. Obst. & Gyn.*, 1938, 35: 810.

Ninety-three per cent of 30 rats kept on a diet defective in vitamin E until they began to resorb their fetuses possessed anti-proteolytic power in the blood serum. Only 11 per cent of 28 rats on normal diets revealed this substance. In 35 per cent of 23 women whose lactation was inadequate during the puerperium wheat germ therapy restored efficient lactation. Some of the therapeutic possibilities of wheat germ oil are indicated. About 15 per cent of abortions are not controlled by wheat germ oil therapy. Failures are discussed. As so many aborted fetuses are deformed, the question arises as to the advisability of wheat germ oil therapy designed to prevent abortions. Statistics are reviewed, and personal experiences recorded, to indicate that such therapy is probably justified.

ROSS MITCHELL

The Action of Sulphanilamide on Brucella Abortus Infections. Manson-Bahr, P.: *The Practitioner*, 1938, 140: 740.

Three well-defined cases of undulant fever successfully treated with sulphanilamide are described. In each case there was a high titre of agglutination for *Br. abortus* and *Br. melitensis*. In two cases there was satisfactory response to the oral administration of 1.5 g. of sulphanilamide daily. In one of these the temperature, which had been of the characteristic undulating type, returned to normal, the palpable spleen also shrinking beneath the costal margin. When sulphanilamide was discontinued after the patient left hospital, fever

returned accompanied by arthritis. Recovery again occurred when sulphanilamide therapy was reinstituted. The third case showed no response to oral administration, but good results were obtained from deep subcutaneous injections of the same drug. In each case the clinical signs and symptoms abated with the temperature. In two of the three cases a fall in the titre of agglutination was observed in the course of treatment.

The author points out that a small bout of fever on cessation of sulphanilamide treatment need not be regarded as a definite relapse, but as the natural termination of infection. Similar rises in temperature are observed in cases not treated with sulphanilamide.

C. R. BOURNE

Radiology and Physiotherapy

Non-routine Views in Roentgen Examination of the Extremities. Lewis, R. W.: *Surg., Gyn. & Obst.*, 1938, 67: 38.

The author shows by diagrams the positioning of patients and the results of these unusual x-ray films. He does not make any claim to originality, but states that the methods have been used by his associates and others. They may be of use to some who are not satisfied with the regular routine films, inasmuch as these fail to fulfil individual clinical intuition. For projections of the shoulder, such as in external rotation of the humerus, he allows the forearm to remain across the epigastrium but turns the trunk into the oblique position. For lateral projection of the humeral head the sound hand is placed on the vertex of the head allowing definition between the thoracic spine and sternum. Vertical projection of the head defines also the acromion, coracoid process, outer end of the clavicle, and calcareous deposits in and about the head. Oblique projections of the clavicle from below are possible; at the same time the acromion is seen. In acromioclavicular separations the erect posture without support of the extremity gives more exact information; "the inferior surfaces are more reliable guides". In "epicondylitis humeri" an oblique view tangential to the posterior surface gives better definition. Lateral views of the flexed and extended elbow define and delimit small calcifications and separation of the olecranon; this may be applicable to old fractures about the elbow and ankle. Oblique views between pronation and supination, respectively, and true lateral show the carpal bones. Vertical projection of the patella may be obtained with right-angled flexion of the knee and the tube directed anteriorly. Postero-anterior projections of the knee give as complete information and show the patella more clearly, and full extension is not necessary to get a good film. Oblique view of the ankle, 45 degrees internal rotation, shows the lower tibiofibular articulation fractures of the tibia, fibula, calcaneus.

astragalus and avulsed spicules of bone by the deltoid, anterior and posterior talofibular and the calcaneo-fibular ligaments. In examining forefeet for the etiology of callus and warts a metal marker is helpful. Full extension of the toes with right-angled ankle can give a good projection for the sesamoid bones.

FRANK DORRANCE

Pathology and Experimental Medicine

Heat Stroke: Clinical and Chemical Observations in Forty-four Cases. Ferris, E. B. Jr., Blankenhorn, M. A., Robinson, H. W. and Cullen, G. E.: *J. Clin. Investigation*, 1938, 17: 249.

In a series of 44 patients suffering from heat-stroke the authors found that cardiac or peripheral circulatory collapse was not evident in the majority. Also the sodium chloride content of the blood was not significantly altered. The condition, however, was associated with a moderate acidosis and hæmoconcentration. The high body temperature appeared to be the chief cause of the symptoms. Old age, degenerative disease, and acute alcoholism were found to be important contributory factors.

Clinically, the authors found that the onset was precipitated by a diminution or cessation of sweating in the majority of the patients. Though they could not actually find the primary cause of the cessation of sweating they thought that loss of electrolytes, dehydration, and circulatory failure were not responsible.

In therapeutics the authors found that ice-water tubbing, with massage, was the most efficacious measure.

JOHN NICHOLLS

The Effect of Epinephrin in Circulatory Collapse Induced by Sodium Nitrite. Wilkins, R. W., Weiss, S. and Haynes, F. W.: *J. Clin. Investigation*, 1938, 17: 41.

These authors studied the effect of epinephrin in vasomotor collapse produced by sodium nitrite. Both in the horizontal and in the upright position epinephrin in subcutaneous doses of 1 mg. caused arteriolar and decreased blood-flow in the hand. The venous tone became increased, as did the arterial pulse-pressure and the heart rate. The venous pressure was usually slightly elevated. But epinephrin did not prevent the vasomotor collapse and syncope produced by sodium nitrite, mainly because the arteriolar constriction and the tissue anoxia were enhanced and because the decreased venous tone produced by the nitrite was not adequately compensated for. The experiments also indicated that the level of arterial pressure is not a reliable index of the clinical manifestations of vasomotor collapse or the degree of tissue anoxia. The authors conclude that though epinephrin is ineffective in collapse produced by nitrite its efficacy in other forms of collapse is not ruled out.

JOHN NICHOLLS

Hygiene and Public Health

Clinical and Neuropathological Aspects of Electrical Injuries. Alexander, L.: *J. Indust. Hyg. & Toxicol.*, 1938, 20: 191.

This article consists of a complete description of the neuropathological lesions in electric shock together with several case reports. An extensive bibliography is appended. A statement regarding artificial respiration, as follows, merits a special note. "Artificial respiration by the prone-pressure method should be started as soon as possible and carried out unceasingly and untiringly for 8 to 12 hours until either spontaneous respiration returns or livid patches and rigor mortis appear." This advice is based upon the conclusion that inhibition of the heart following shock may be incomplete, and that tissues may remain vital by a slight amount of circulation maintained by feeble cardiac contractions, possibly for several hours.

FRANK G. PEDLEY

Chronic Lung Changes in Electric Arc Welders.

Enzer, N. and Sander, O. A.: *J. Indust. Hyg. & Toxicol.*, 1938, 20: 333.

An examination of 26 men engaged in arc-welding steel tanks showed 5 with definite nodulation of the lungs similar to silicosis and 5 with exaggerated lung markings. Sixteen had negative lungs. The possibility of a silicosis exposure is very remote. An autopsy performed on one of the men with nodulation who had died of pneumonia indicated that the nodulation was probably caused by a deposit of iron oxide. There was no evidence of functional impairment of the lungs and no indication of tuberculosis.

FRANK G. PEDLEY

Obituaries

Dr. William Clinton Acheson, of Vancouver, died about the beginning of May, aged seventy-three. He was born in Ontario and went to British Columbia in 1893. He was a graduate of the University of Toronto (1907). He practised in Vancouver from 1909 until his retirement a few months ago.

Dr. Annie Amelia Backus, one of the first women physicians in Ontario, died at Port Rowan, Ont., in her seventy-sixth year. Dr. Backus was born in Yorkshire, England, the daughter of the late J. H. Backus and Sarah Dedrick, pioneer settlers in Ontario. She received her early education at Port Rowan, a private school at Simcoe, and graduated from the Hahnemann Medical College, Chicago (1889). She did considerable research work abroad and became known as a child specialist, practising in Ann Arbor for 10 years, and later in Aylmer for 15 years. She married Albert Backus, a prominent Aylmer lawyer, while practising there. In her later years she was a lecturer in Women's Institute work, covering the province in her tours. Deceased had resided in Port Rowan for the past 23 years. Her husband died 17 years ago.

Dr. Bertram Cameron Blackhall, of Toronto, died on June 8th, in his twenty-ninth year. Born in Kingston, Ont., in 1909, he was the only son of Mrs.

Lillian B. Blackhall and the late Bertram Blackhall. He received his education at the University of Toronto Schools, Oakwood Collegiate and the University of Toronto, from which he graduated in 1935.

Dr. Frederic Boulanger, of Ste. Agathe de Lotbinière, Que., died on July 6, 1938, in his seventieth year. He was a graduate of Laval University, Quebec (1894).

Dr. William Allen Cathcart, of Wallaceburg, Ont., was killed instantly in an automobile accident on June 7, 1938. The late Dr. Cathcart was a son of the late William A. Cathcart and Mrs. Fannie Cathcart of Courtright. He was 46 years of age and a native of Courtright. He attended the district schools and took his medical course at University of Toronto where he graduated with honours in 1915. He took over the practice of his brother, Dr. Selby Cathcart at Port Lambton and several years later he married Dr. Bessie Culver of Simcoe who was associated with him in his profession for many years. About three years ago they moved to Wallaceburg and have since resided there. For many years he was medical officer of health for Sombra township.

Dr. Thomas J. Costello, a member of one of Calgary's pioneer families, died at his home, on July 8, 1938, at the age of fifty-seven years.

He was born in Renfrew, Ont. and was only two years of age when his parents moved to Calgary. Following his graduation from Ottawa College he took his medical course at Queen's University. He spent two years as intern at the Water Street Hospital, in Ottawa. He practised in Calgary from 1907 until shortly after the beginning of the War. He served in the far east with the Royal Army Medical Corps. On his return to Calgary after demobilization he resumed practice. In 1922 he joined the British colonial service and became medical officer at St. Kitts, West Indies, which post he retained until 1936, when he suffered a severe heart attack. He returned to Calgary in 1937. He is survived by his widow. His brother, Dr. M. C. Costello, former mayor of Calgary, predeceased him.

Dr. Allan Rupert Cunningham, aged 58, of Halifax, Nova Scotia, died suddenly at Saranac Lake, New York, on July 3, 1938. Dr. Cunningham had been under treatment at the sanatorium for some months past, but was making excellent progress and his death came as a shock to his many friends.

Dr. Cunningham was a son of the late Dr. and Mrs. N. M. Cunningham. He took an Arts degree from Dalhousie University and, in 1904, his degree in medicine. After post-graduate studies in England and on the continent in diseases of the eye, ear, nose and throat, he took up practice in Halifax. He was successful and popular in his chosen work, taking, too, an active interest in yachting at the Royal Nova Scotia Yacht Squadron where he served as Vice-Commodore during his last year.

He was a member of the surgical staff of the Victoria General Hospital, a Fellow of the American College of Surgeons, a member of the local medical societies and of the Canadian Medical Association. He leaves his wife, his daughter, Betty, and two sisters, Miss Katherine Cunningham, Winnipeg, and Mrs. Peter McCurrach, Kamloops, B.C.

Dr. Joseph Louis Easton, of Ayrton, Ont., died on May 5, 1938. He was born in 1868 and a graduate of the University of Toronto (M.B., 1898).

Dr. Adelard Falardeau, formerly of Ottawa and Hull, died at his home in Fournier, Ont., on June 7, 1938. He was in his fifty-second year, and had practised medicine at Fournier and the surrounding district for

the past 14 years. Born at Hull, he was educated in Hull schools and McGill University, from which he graduated in medicine (1921). During his career he practised in Ottawa for some years, and later in St. Joseph d'Orléans, prior to moving to Fournier.

Dr. John Bell Fraser, of Toronto, died on May 25, 1938, in his eighty-third year. He was born at Mill Creek, Ont., and received his primary education at Sharpton public school. He was a graduate of Queen's University and Trinity University (1888).

Dr. John Albert Gallagher, of Toronto, died on May 7, 1938, in his sixtieth year. He was a graduate of the University of Toronto (1905.) Born near Alliston, Dr. Gallagher attended school there, and later entered the University of Toronto. While studying there he operated a drug store at Sackville and King Streets. He later ran a drug store at Jones Avenue and Gerrard Street.

Dr. Gallagher took post-graduate work in London, England, and on his return to Toronto set up in practice, specializing in obstetrics. After practising there for many years he became interested in the building industry, and was responsible for the erection of more than 400 houses in the city.

Dr. Thomas Sylvester Kirby, of Cartier, Ont., died on May 3, 1938. The late Dr. Kirby had practised his profession in Cartier for the past nine years, going there from Levaack. He was educated in the separate and high schools at Arthur, and, in 1910, graduated from the University of Toronto medical school. He was born at Drayton, Ontario, 52 years ago, the son of the late Mr. and Mrs. Patrick M. Kirby.

Dr. Allan James MacKinnon, of Zurich, Ont., died on March 18, 1938. He was born in 1874, and a graduate of the University of Toronto (1908).

Dr. Manole Don Moyse, of Waterloo, Que., died on June 28, 1938. Dr. Moyse was born in Bucharest, Rumania, 43 years ago, and came to this country with his parents when he was 14. He was educated at the Montreal High School and at McGill University, graduating in 1920. After post-graduate work in New York and a year spent at teaching pharmacology at McGill, he took up the practice of medicine at Waterloo.

Dr. Wilfrid C. Pepin, of Windsor, Ont., died on May 22, 1938, at the age of fifty-four. Dr. Pepin was born in Windsor, the son of the late Mr. and Mrs. Joseph Pepin, pioneer residents of the county. He graduated from St. Alphonsus Separate School and the old Windsor Collegiate. He graduated in medicine from the Wayne University Medical College, Detroit (1906). He had practised in Windsor for nearly thirty years.

Dr. Moses Chesley Roberts, of Toronto, died on May 23, 1938. He was born in 1879, in Newfoundland, and was a graduate of McGill University (1911). He took a post-graduate course in Vienna and Budapest.

He served overseas during the Great War and after the armistice returned to Canada, taking up residence in Regina. He practised there for about five years before coming to Toronto. He was associated with St. Joseph's Hospital.

Dr. Frederick Winnett, of Toronto, died on June 16, 1938. Dr. Winnett had practised medicine in Toronto for nearly 50 years. Born in London, Ont., he later attended the University of Toronto, graduating in 1889. He became a member of the Royal College of Surgeons in 1890, and practised in Toronto from that date.

News Items

British Columbia

The radium which has been acquired by the British Columbia Cancer Foundation is now being processed to be put into use at an early date. One gram will be used in the form of needles, while it is proposed that the remaining two and one-half grams will be utilized as a bomb at a later date.

The Pacific Coast Oto-Ophthalmological Society held its Annual Convention at the Empress Hotel in Victoria from June 21st to 23rd. The attendance was excellent and a number of important and instructive papers were presented by visiting speakers. The annual golf tournament was held at the Oak Bay Links and among the winners Dr. R. Scott-Moncrieff, of Victoria, received the Puget Sound Cup for the best gross score. The meeting terminated with a banquet at the Empress Hotel.

Among 138 deaths from notifiable diseases occurring in British Columbia during the month of April 76 were from cancer.

The Health Insurance Act has come under notice again in connection with an address by Mr. Hugh Wolfenden, a widely known consulting actuary and statistician, delivered before a conference on social work lately. In reviewing legislation passed in this province, he found that the benefits to be offered in return for the contributions were in reality almost wholly undefined. He also observed that the prerequisite to any plans of this nature was a "clear and honourable agreement with all those indispensable groups—doctors, nurses, druggists, hospital officials and laboratory technicians" without whose cooperation any such plan must be foredoomed to failure. He would have control of the plan in the hands of a non-political commission "of practical and fully-qualified men, thoroughly experienced in medicine, insurance administration, claim supervision and finance."

The Vancouver Medical Association Summer School was held in Vancouver from June 21st to 24th. The attendance was large, the speakers well selected, the entertainment was skilfully arranged and perfect summer weather continued throughout the week. The visiting speakers were Dr. Ray F. Farquharson, from the University of Toronto, Department of Medicine; Dr. Andrew Hunter from the University of Toronto; Professor of Pathological Chemistry, Dr. Oliver S. Ormsby, Professor of Dermatology at the Rush Medical College, University of Chicago; Dr. R. Glen Spurling, Associate Professor of Surgery at the University of Louisville, Ky., and Dr. Waltman Walters, Professor of Surgery at the Mayo Clinic, Rochester, Minn. At a luncheon held on the opening day the address was by Dr. Andrew Hunter, who spoke most entertainingly with the assistance of numerous lantern slides on "The Edinburgh School of Medicine; historical notes and personal recollections." The golf tournament was held at Jericho Golf and Country Club and a large number of competitors appeared.

D. E. H. CLEVELAND

New Brunswick

Dr. L. DeV. Chipman, of Saint John, has been granted an honorary life membership in the Canadian Red Cross Society for exceptional services rendered it.

Dr. E. W. Ewart has established a practice in orthopaedic surgery at Moncton.

Dr. E. C. Menzies, Superintendent of Provincial Hospital, at Fairville, was granted a fellowship recently in the American Psychiatric Association.

Dr. Charles McMillan, Saint John, has been elected President of the New Brunswick Musical Festival Organization for the third successive term.

Dr. W. W. and Mrs. White, of Saint John, recently celebrated their forty-fifth wedding. Dr. White is convalescing satisfactorily from a long serious illness, which has confined him to his home.

The medical profession of New Brunswick was represented at Halifax by a very large delegation who attended the meetings of the Canadian Medical Association. They all report an excellent program and a very fine holiday.

Lieut.-Col. R. A. Hughes, District Medical Officer of Medical District No. 7, reports that at Camp Sussex this year all military units are taking in their own medical officer, and the 14th Field Ambulance, under the command of Lieut.-Col. V. D. Davidson, E.D., will have a greater number of officers and men under canvas this year than several years past.

Col. A. E. Snell visited various centres in New Brunswick lately in the interests of the Saint John Ambulance Association.

Dr. Merrill Cruickshanks, O.B.E., Medical Administrator of Nassau, Bahamas, has this month been visiting his old home at Saint John. Dr. Cruickshanks is on his way to do post-graduate work in Great Britain.

A. S. KIRLAND

Nova Scotia

Two thousand dollars has been promised by the Red Cross Society, to erect an outpost hospital in north Cape Breton, which, during the winter months has at times been completely cut off from the larger southern centres.

Dr. W. E. Murray (Dalhousie '37) has been appointed house physician to the Nova Scotia Hospital at Dartmouth. Dr. Murray has been practising in Truro.

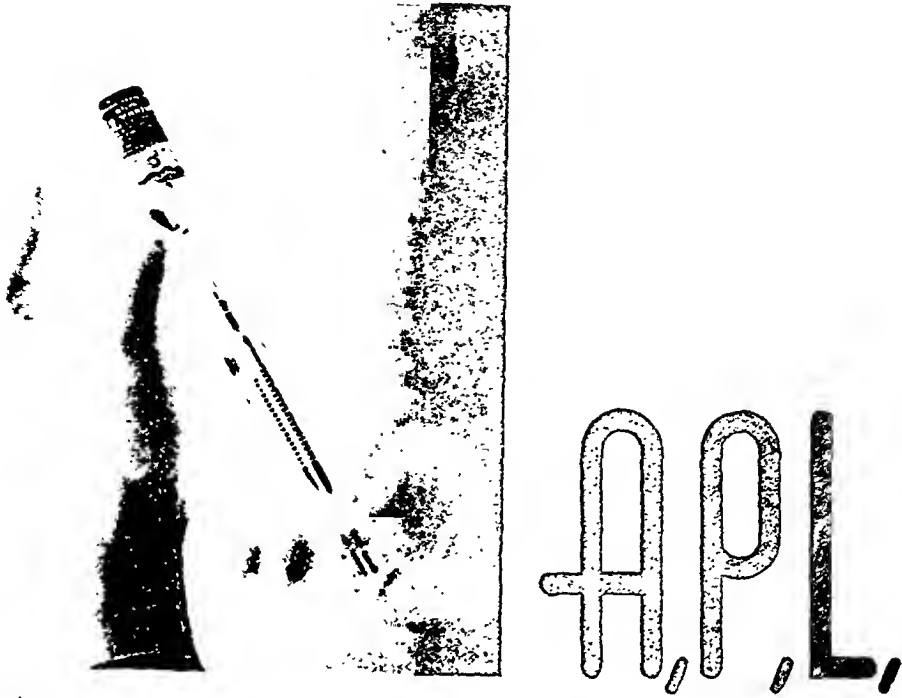
Dr. George W. A. Keddy with his bride arrived home from Edinburgh. Dr. Keddy has been studying on the continent and in Scotland since his graduation from Dalhousie in 1935.

A plan for cooperative medicine, to work in conjunction with the Extension Department of St. Francis Xavier University, was introduced at a meeting of the board of directors of the Dominion Credit Union recently. This would apply in the rural communities where the extension work has proved its worth in cooperative buying and saving schemes and in the education of the members toward the better understanding of their crafts. It was suggested that the various study clubs in the communities take up the problem from their respective points of view before completing the plans.

Dr. Laurie Teasdale, of Dartmouth, has sailed for England and the continent where he plans to continue his post-graduate studies in oto-laryngology. With him went his bride, the former Miss Dorothy Mitchell, of the staff of the Montreal General Hospital.

The new tuberculous annex of the Highland View Hospital, Amherst, was formally opened to the public by Hon. F. R. Davis, M.D., Minister of Health.

A further grant of \$5,000 from the Rockefeller Foundation has been made to extend the survey of



rational therapy for cryptorchidism

"Sufficient clinical evidence is at hand to indicate that endocrine therapy alone is capable of bringing about the descent of a cryptorchid testis in about 50 per cent of all cases. It is useful in identifying those testes which cannot be expected to descend at puberty and which, therefore, should be operated on at an earlier age. When operative procedures for the condition become necessary, the preliminary gonadotropic therapy facilitates surgery by elongating cord elements, and, lastly, the postoperative results are greatly improved by the endocrine treatment." *Editorial: Endocrine Therapy of Cryptorchidism, Jour. A.M.A. 110: 288-289 (Jan. 22) 1938.*

A.P.L.—the chorionic gonadotropic hormone—is biologically standardized after the technique of Dr. J. B. Collip, McGill University.

No. 463 in 5 and 10 cc. vials

No. 463—500 rat units (Collip) per cc.

No. 450 in 5 and 10 cc. vials

No. 450—100 rat units (Collip) per cc.

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Biological and Pharmaceutical Chemists
MONTREAL

CANADA

morbidity carried out in Cape Breton by the Institute of Public Affairs of Dalhousie in cooperation with the Department of Epidemiology. ARTHUR L. MURPHY

Ontario

The St. John's Convalescent Hospital, Toronto, has completed its first year of work. Built to accommodate 65 patients it has already outgrown its capacity and could fill double its present number of beds.

Work has begun on the alterations being made to the Penetanguishene General Hospital.

The Brantford Council has at last given a third reading to the long deferred By-Law providing for the issue of debentures amounting to \$150,000 for the erection of a 64-bed addition to the Brantford General Hospital.

In June tenders were called for the new Nurses' Home at the General Hospital, Port Arthur. This building will accommodate about 45 nurses and staff members of the Hospital.

A new wing to cost \$15,000 will be added to the St. Andrew's Hospital, Midland.

We are told that an addition to cost \$100,000 is to be made to the Chatham General Hospital.

The Queen Alexandra Sanatorium at London, Ontario, has been bequeathed the sum of \$8,000 by the late A. J. Doggerell, who was their first auditor and continued in this position up to the time of his death.

The Collingwood General and Marine Hospital celebrated its Fiftieth Anniversary of its founding in May, 1938.

Dr. B. T. McGhie, Deputy Minister of Health, has announced a joint appeal to the public by the Departments of Agriculture, Education, and Health, to undertake netive measures for the destruction of ragweed which, formerly limited in its distribution, has now become widespread throughout the whole of Ontario south of Magnetawan. Along the lines of motor traffic and railway, it has now established itself much farther north.

Dr. W. T. Noonan, of the staff of St. Michael's Hospital, has been elected a Fellow of the Royal College of Physicians of Ireland.

Dr. Howard Justus (Queen's, 1926) has been appointed resident physician of the Cornwall Sanatorium, of which Dr. George W. Cragg is the Medical Superintendent.

Dr. W. D. Smith has retired from general practice in the town of Creemore to accept a position on the staff of the Ontario Mental Hospitals, and was the guest of honour at a complimentary banquet given him by his friends on May 13th. He was presented with a gold watch and was the recipient of many expressions of appreciation for his active interest in the progress of his community during his long period of practice.

Dr. J. T. Finney, Jr., of Baltimore, addressed the May meeting of the Essex County Medical Association.

The York Township Medical Association has instituted a drive for the purpose of raising funds for the building of a hospital to serve Forest Hill, Northwest Toronto and York Township.

The new wing of St. Joseph's Hospital, Parry Sound, was officially opened on April 20th. The building is a three story, fireproof structure and is the latest in hospital construction and equipment.

Lt.-Col. L. J. Austin and B. H. Hopkins were awarded on April 1st the Royal Canadian Efficiency Decoration.

Dr. L. G. Rowntree, of Philadelphia, has been presented with the Dr. I. P. Strittmatter Gold Medal for meritorious service redounding to the credit of the medical profession.

The Royal College of Physicians, London, announced on April 28th election to fellowship in the College of Prof. H. S. Raper, C.B.E., D.Sc., M.B., F.R.S., formerly of the Faculty of Medicine, University of Toronto, and Prof. J. B. Collip, D.Sc., M.D., F.R.S.

On May 19th, Dr. Wm. H. Tytler (Toronto, 1939), research bacteriologist of the Welsh National Memorial Association, was appointed to the David Davis Chair of Tuberculosis in the Welsh National School of Medicine of the University of Wales, to succeed to the vacancy created by the retirement of Prof. S. Lyle Cummins.

The post-graduate medical week early in June at Hamilton was an outstanding success. Inaugurated one year ago, it was so successful that an extra day was added this year. There was a registration of 550 doctors who came from almost all parts of the province. The meeting was practically of a clinical nature carried on at the General Hospital. The pathological exhibit under the direction of Dr. W. J. Deadman attracted much favourable comment. The officers and members of the Hamilton Academy of Medicine and of the General Hospital are to be congratulated upon the result of their carefully prepared program of post-graduate instruction.

Dr. F. B. Plewes (Toronto, 1934) has been appointed a Fellow of the Royal College of Surgeons of Edinburgh.

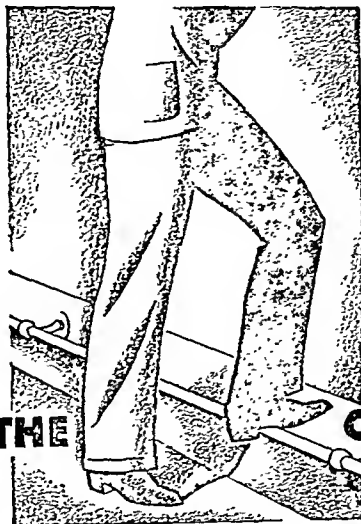
The *Canadian Hospital* for June carries a splendid illustration of the new building for the Toronto Hospital for Consumptives, Weston. It is a fine brick structure of five stories and basement providing 180 beds. Approximately half of these are to replace some of the older pavilions. The remainder will be additional beds and will bring the total capacity of this hospital to 666 beds. There is also an architect's sketch of the new Wilcox Pavilion, the first sod for which was turned recently at the Mountain Sanatorium, Hamilton.

It is also announced that the new mental hospital at St. Thomas when completed will comprise 36 buildings, occupy and utilize 1,100 acres of land, and accommodate 2,300 patients. The total cost it was stated will be in the neighbourhood of \$8,000,000. Two units will segregate the male and female patients; each pavilion in these units will accommodate 210 patients. The recreation hall will seat 1,000 and will be equipped with stage and motion picture equipment.

J. H. ELLIOTT

Quebec

Dr. Fraser B. Gurd, of Montreal, has been chosen as Vice-president of the newly formed American Association of Traumatic Surgeons. The first meeting of this body was held in San Francisco recently. Dr. K'llogg Speed, of Chicago is President.



AMONG THE CAUSES OF HYPERACIDITY

Certain disorders almost invariably, but certain "habits" not much less frequently, are the prolific source of gastric hyperacidity. The "last" drink of liquor, that additional cup of coffee, another pipeful of tobacco, rich food that pleases the palate but displeases the stomach, fear and worry—all must share the blame of mischief-making in the stomach.

Pointing out the error of the patient's mode of life and habits may be a preventive of excess acidity in the stomach, but for the prompt relief of the pain and discomfort attending it CAL-BIS-MA supplies the answer. Cal-Bis-Ma accomplishes gastric neutralization promptly and its effect is prolonged. Secondary acid rise and gaseous distention are prevented by its soothing, sedative, protective and adsorbent properties.

Why not ask us to send you literature and a trial quantity of Cal-Bis-Ma? It explains the composition, points out the uses, and lets you test the value of Cal-Bis-Ma by the best judge—yourself.

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Powder obtainable in tins of 1½ and 4 ounces.

William R. Warner & Co., Ltd., 727 King Street, W., Toronto, Ontario

Book Reviews

Health and Unemployment. L. C. Marsh, A. G. Fleming and C. F. Blackler, McGill University, Montreal. 243 pp., illust. \$2.50. Oxford University Press, Toronto, 1938.

The basic assumption of this volume is "that there are direct relationships between the employment status of individuals, families, or communities, and the prevalence of and duration of illness". In an effort to show the extent of these relationships and obtain some definite measurements of the effect of unemployment on the population, the authors take us through a detailed statistical analysis of sample groups of male adults, male minors, and families in Montreal affected by unemployment in the depression years. The treatment is detailed and the limitations of the samples and results are adequately noted. These features add to rather than detract from the importance of the findings since investigation in this field is only beginning in Canada. Consideration of effects of unemployment on families leads to a discussion of costs of adequate minimum nutrition in relation to the relief allowances granted in different Canadian cities. Charts and tables are numerous. Some of the percentages derived from small samples are possibly too "accurate". In a tabulation on page 112, 4 out of 35 is listed as 11.4 per cent, and 4 out of 37 as 10.8 per cent. Perhaps neither of these should be refined beyond 11 per cent. Another example of over-refinement is noticed in a table of emergency calory standards for daily diets quoted from an American source. The requirement for a moderately active man is given as 3,021 calories and for a very active man 4,286.

The last part of the study deals with efforts that have been made to date to extend medical care to sections of the population who cannot themselves afford the cost involved in its unequal incidence. This section is, perhaps, the most interesting. A close study of the preliminary statistical portion of the book is necessary, however, to appreciate what is involved in the problem and the value of the different remedies and palliatives being used and under consideration. The place and value of medical relief, the difficulties inherent in establishing health insurance, the "community" or "municipal" doctor system, and various other methods for group medical care and hospitalization are reviewed. Due attention is paid to the distinguishing characteristics of rural and urban phases of the problem. The author's initial assumption may be restated by saying that lack of health has tended to be a corollary of lack of wealth. This has often been listed among the charges against capitalism. All the remedies here outlined for the situation are attempts to provide an adequate basis for health and medical care by sharing of the cost, voluntarily or compulsorily through taxation. Whatever solution is adopted, it cannot help but be socialistic in nature; yet even the most diehard individualist who studies the data, conclusions, and possibilities outlined in this book will realize the national good that would be achieved if a basis were found whereby the health of the Canadian became independent of his economic status.

The authors are to be congratulated on an able survey of a complicated subject.

British Encyclopædia of Medical Practice. Edited by Sir Humphry Rolleston. Vol. 5, 632 pp., illust. \$10.00 a vol., Butterworth, Toronto, 1937.

This volume opens with a capital article on Endoscopy of the upper respiratory and alimentary tracts. There are excellent illustrations of various phases of this work. This is followed by a chapter on Endoscopy of the urinary tract. The section on Typhoid compresses a great deal into a short space. Perhaps a little more might have been said with regard to typhoid carriers

and their importance in sporadic outbreaks, especially in institutions. In the chapter on Epilepsy there is no mention of allergy as a possible causative element. The account is otherwise compact and complete. The chapter on Food is of considerable interest. It shows a commendable caution in estimating our knowledge regarding the chemistry of vitamins and foods. We have no reliable tests for detecting anything more than minor degrees of deficiency, but in time we may hope to be able to state vitamin intake and requirements in terms of units.

The Heart in Pregnancy. J. Jensen. 371 pp. \$6.50. McAinsh, Toronto, 1938.

The author presents in this book a most extensive review of the medical literature on the heart in pregnancy, 26 pages being required for the tabulation of references. As the author states in his preface, the book represents a stock-taking of our present knowledge of this important subject. The material is well arranged and presented. A tendency to too great length and detail of discussion is compensated for by short summaries at the end of each section. The first part of the book, discussing "The effect of pregnancy on the normal heart" is of particular interest and value to both cardiologist and obstetrician and emphasizes the need for further study and research in the physiology of the heart during pregnancy. The problems of rheumatic heart disease and pregnancy form the second main division of the book. The chapter on the management of pregnancy in rheumatic heart disease is extremely valuable, the author expressing his own views, which he fails to do in most sections. The indications for termination of pregnancy, which are always controversial, show a conservative tendency on the part of the author and some of his statements in this section are open to serious question. The same conservative advice is given in regard to sterilization. The question of sterilization is summed up by the rather unusual statement "that before deciding to sterilize a woman it should be reasonably certain that she will never be so situated that she will be able to or desire to have more children".

The use of Cæsarean section as a means of delivery of patients suffering from heart disease is fully discussed and the trends in its use in America and Europe are pointed out. The last part of the book discusses non-rheumatic heart disease and pregnancy, the chief sections being bacterial endocarditis, cardiovascular syphilis, congenital and degenerative heart disease. The review and summary of the literature in this section is of particular value as these lesions are not nearly so frequently encountered as rheumatic lesions, and any individual's experience in their management is limited.

Leukæmia and Allied Disorders. C. E. Forkner, A.M., M.D. 333 pp., illust. \$5.00. Macmillan, Toronto, 1938.

This book offers a complete review of the literature on the leukæmias and fills the need for a comprehensive monograph on these obscure diseases. Whether the reader is interested in the historical, clinical, pathological or experimental aspects of leukæmia, he will find here an excellent summary of the available information. During the preparation of the manuscript more than 5,000 references were consulted and 1,600 of these are cited in the bibliography. The author is a practised writer and presents his subject in a pleasing manner. The book would be more attractive if printed in larger type.

A Textbook of X-ray Diagnosis. Edited by S. C. Shanks, M.D., P. Kerley, M.D., M.R.C.P., D.M.R.E., and E. W. Twining, M.R.C.S., D.M.R.E. Vol. 1, 598 pp., illust. 50s. Vol. 2, 458 pp., illust. 42s. H. K. Lewis, London, 1938.

Volume one deals with the cardiovascular system, the chest and the urinary tract. The cardiovascular section deals with technique and interpretation in

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orthodiagraphy, cineradiography and roentgen-kymography and arteriography. The section on the urinary tract describes the preparation of the patient and radiographic technique and interpretation of findings in urography.

In the second volume radiological examination of the alimentary tract is presented in considerable detail and contains accurate descriptions of almost every conceivable gastro-intestinal lesion. The section on cholecystography, both oral and intravenous methods, is well handled and presents accurate descriptions of technique of cholecystography and of interpretation of results. Modern conceptions of radiology in obstetrics are well presented in the last section of the second volume.

Throughout both volumes the subject matter is particularly well handled; the text clear and concise and thoroughly up-to-date. Every modern diagnostic method is described in detail and the criteria of diagnosis are pointed out. The text is profusely illustrated in both volumes with positive prints of x-ray films and by line drawings. The index is so arranged that the volumes may be used for ready reference and each section of the book is followed by a very extensive bibliography for further reference. These volumes are a truly outstanding modern work on x-ray diagnosis and should be on the book shelves of every man doing diagnostic radiology.

Hernia, Anatomy, Etiology, Symptoms, Diagnosis, Differential Diagnosis, Prognosis, and the Operative and Injection Treatment. L. F. Watson, M.D. 2nd ed., 591 pp., illust. \$8.50. McAlinsh & Co., Toronto, 1938.

The first edition of this work was a worthwhile book. It has been improved and enlarged in the second. Emphasis is placed upon the indications for and the technique of treatment by injection of sclerosing fluids. Experience and increasing skill have widened the field of this method, and there is a well tempered enthusiasm in its presentation. The subject of "sliding hernia", so often dismissed in a page or two of generalities, is here handled adequately. The bulk of the work deals with the commoner varieties of abdominal herniæ, but the rarer forms are well covered.

Brief historical notes at the beginning of each chapter add an interest that makes these short paragraphs a very pleasing addition to the text. Each chapter ends with a full list of references.

The illustrations consist largely of drawings by W. C. Shepard which serve their purpose excellently. The index is well made and cross references make it very useful. It seems to be very complete, but Narath's hernia is described in the text and not mentioned in the index. The book is well written in didactic style, and is to be recommended to surgeons and especially to teachers of surgery.

Speech Training for Cases of Cleft Palate. M. C. Oldfield, M.Ch., F.R.C.S. 20 pp., illust. 4s. 6d. H. K. Lewis, London, 1937.

This booklet is intended not only as an aid to the speech trainer but also as a guide to parents and adult patients. The author wisely stresses the importance of speech training following cleft-palate operations, and states that it should be carried out daily if possible. Various exercises for improving the action of the palate are first given. This is followed by a classification of speech sounds. Each individual sound is then taken up, giving the method of production and the position of the organs of speech for each. The latter is well illustrated by diagrams.

Glaister's Medical Jurisprudence and Toxicology. 6th ed., edited by J. Glaister, M.D., D.Sc. 747 pp., illust. \$7.50. Macmillan, Toronto, 1938.

Glaister's Medical Jurisprudence and Toxicology has achieved a notable position among works of its kind in Britain and the Empire. Written originally for the student, its exhaustive index makes it a ready reference book for the practitioner who may have to seek

assistance in medico-legal cases. In the present edition many chapters have been recast and new matter introduced, including such subjects as dermal and palmar prints, the identification of mutilated and dismembered remains, the identification of fibres, sectioning of hairs, and blood-grouping. Changes and additions are noted also in the section of toxicology. The new edition maintains the high standard of the previous editions as the physician's medico-legal guide.

A Biological Approach to the Problem of Abnormal Behaviour. M. Harrington, M.D. 454 pp. \$4.00. Science Press Printing Co., Lancaster, Pa., 1938.

In this book Dr. Harrington presents the problem of abnormal behaviour from what he calls the physiological point of view. He thinks of behaviour as due to the action of an anatomical mechanism, which developed in the course of organic evolution because it was of value in the struggle for existence, and he explains the occurrence of abnormal forms of thought, feeling, and action as due to the defects and limitations of this anatomical mechanism. He describes his approach to the study of psychology as "mechanistic" in contrast with the current methods of studying psychological problems in terms of motive and desire, which he terms "motivistic". The book is divided into three parts the first of which is concerned with basic concepts and methods, problems of free-will, and consciousness. In part two the mechanism of behaviour is discussed in considerable detail, largely from the standpoint of neurophysiology. The last part of the book is devoted to a discussion of psychopathology.

The manner in which the author presents what he describes as a new approach to the study of abnormal behaviour, and particularly the presentation of the factual material which he utilizes primarily in an attempt to refute the current psychological concepts should make this book a valuable addition to the recent literature on this subject.

Medical Writing. J. H. Dempster, M.A., M.D. 168 pp., illust. \$2.50. Bruce Publishing Co., St. Paul, Minn., 1937.

There are many books on the technique of medical writing but another one will be useful as a reminder. There is no essential difference between good medical writing and any other kind of good writing. Both must be clear, even though they may express widely different thought. That point is well brought out in this book. The chapter on "The Editorial Function" is a little out of the ordinary, and contains some useful and illuminating comments. The other chapters deal with the usual technical details of preparing papers, such as illustrations, references, the manuscript, type and proof-reading, etc. A final chapter describes copyright regulations, and an appendix suggests certain books on writing which may be read with profit. This book will be useful and interesting to all who prepare papers.

BOOKS RECEIVED

Cellona Technique. 69 pp., illust. 4th ed. Issued to medical and veterinary professions only. T. J. Smith & Nephew, Ltd., Hull, England, 1938.

The Traffic in Health. C. Solomon, M.D., Assistant Clinical Professor of Medicine, Long Island Clinic of Medicine. 393 pp. \$2.75. Navarre Publishing Co., New York, 1937.

Ideal Weight. W. F. Christie, M.D. 110 pp. \$1.50. Macmillan, Toronto, 1938.

Malnutrition the Medical Octopus. J. P. Sutherland, M.D., Sc.D. 368 pp. \$3.00. Meador Publishing Co., Boston, 1938.

Milestones in Medicine. Laity Lectures of New York Academy of Medicine. 276 pp. \$2.25. D. Appleton-Century Co., New York, 1938.

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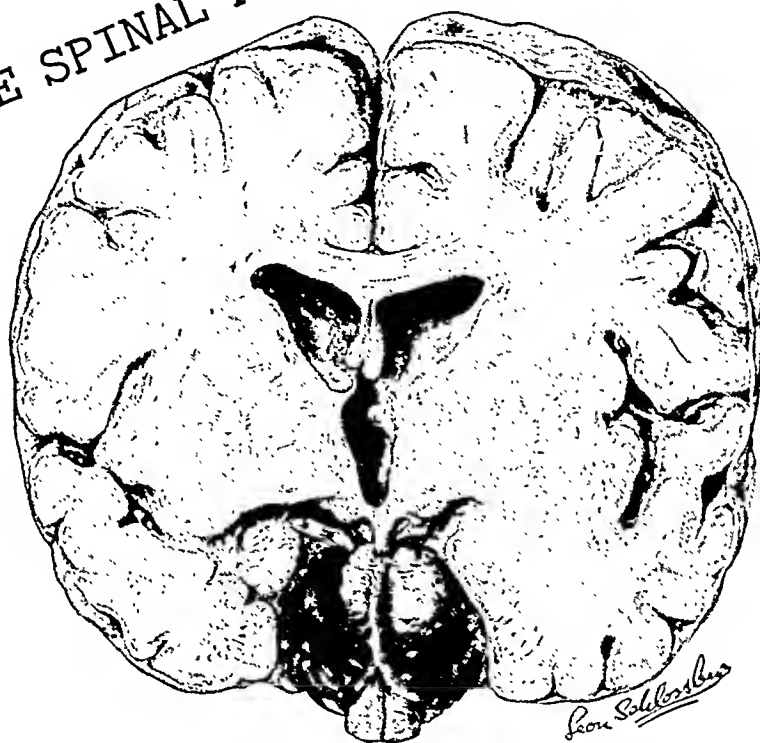
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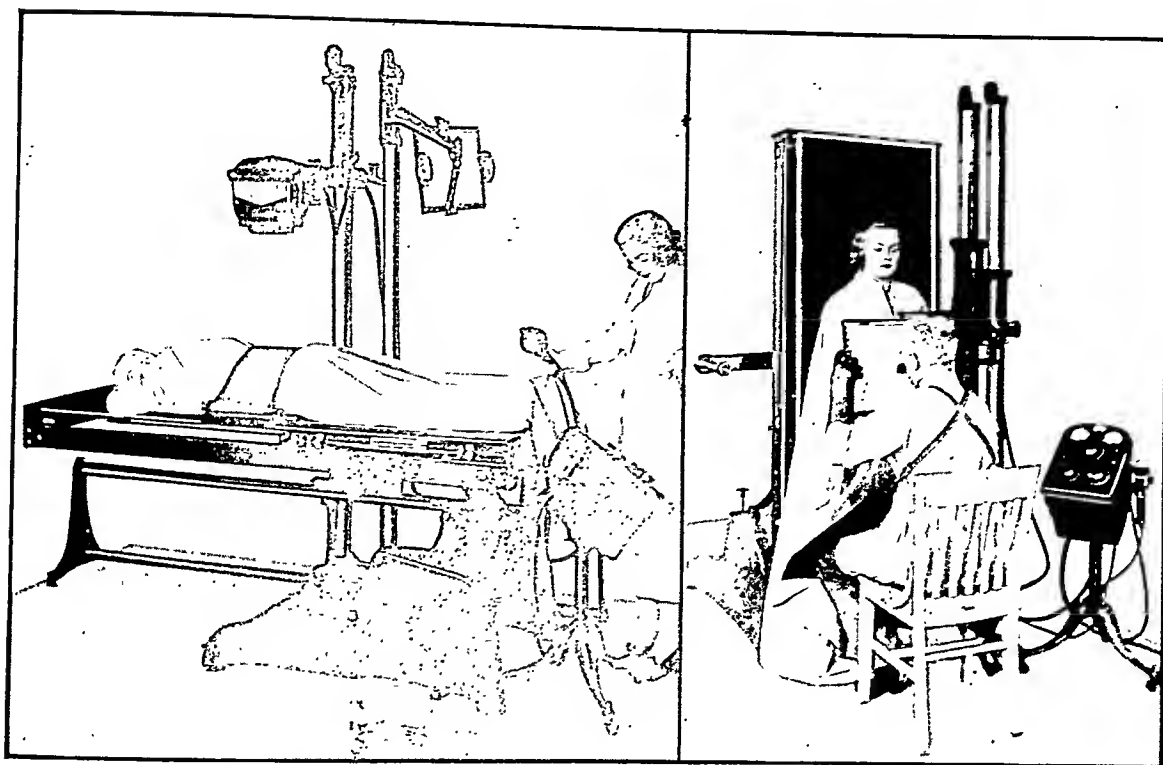
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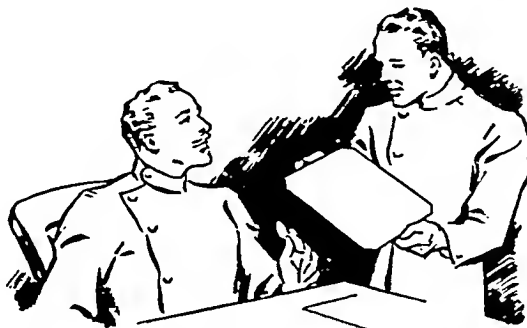
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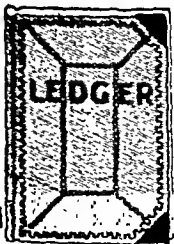
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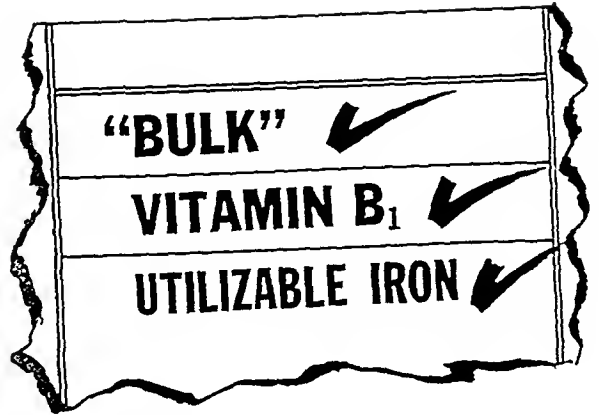
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*CORCORAN,
New York State Journal
of Medicine, Jan. 1, 1930

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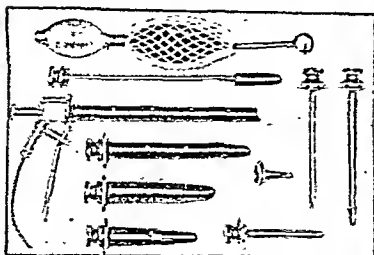


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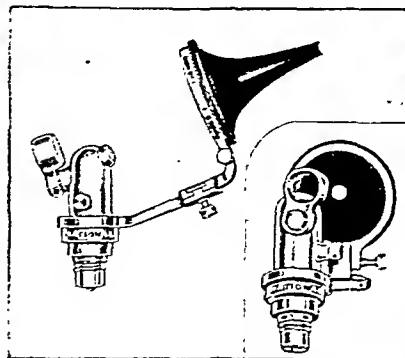
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1a. 1934. J. Amer. Med. Assn. 102, 892.

b. 1936. Ibid. 106, 996.

c. 1937. Ibid. 108, 7 and 15

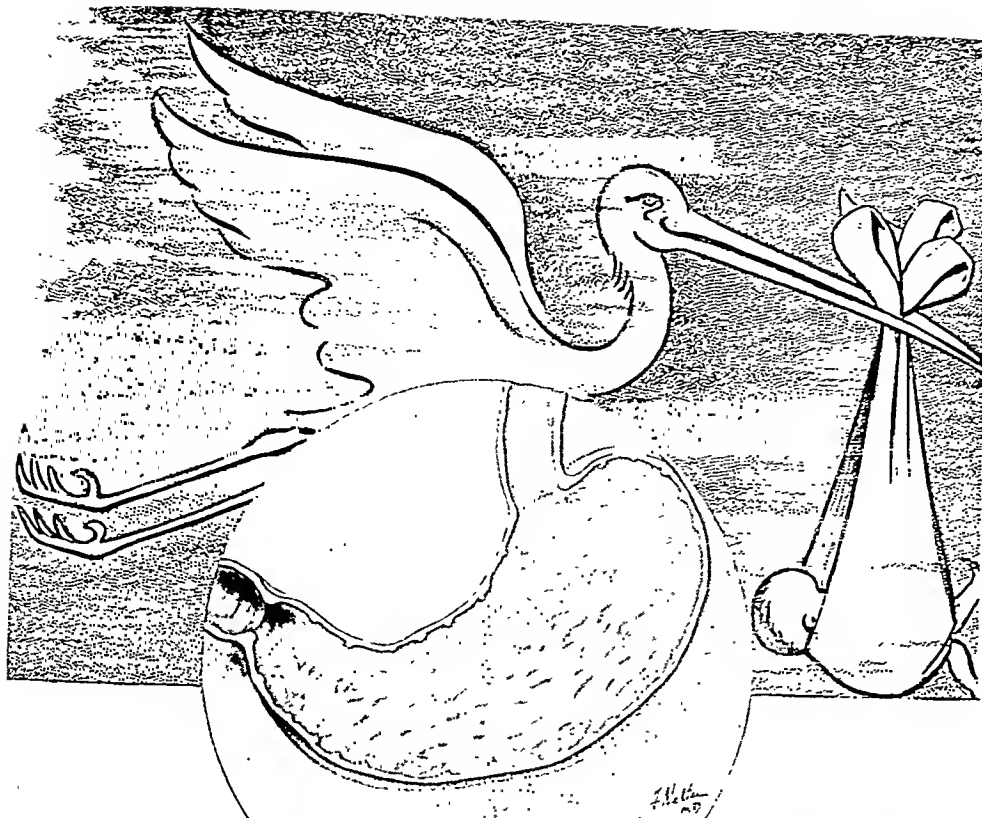
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1935. Amer. J. Public Health 25, 1340.

d. 1937. Ibid. 109, 756.

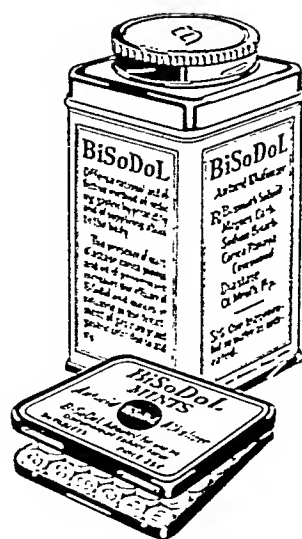
2. 1931. J. Nutrition 4, 267



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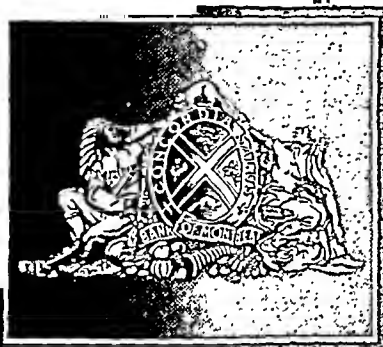
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The Primary and Final Examinations leading to the Diploma of Fellow will be held on the following dates:—

Written Examinations in both the Primary and Final subjects on October 3rd, 4th and 5th—in Vancouver, Edmonton, Saskatoon, Winnipeg, Toronto, Montreal, Quebec City, Halifax.

Oral Examinations in the Primary subjects on October 20th in Winnipeg and October 22nd in Toronto.

Oral and Clinical Examinations in the Final subjects on October 24th in Winnipeg and October 26th in Toronto.

Oral and Clinical Examinations in the French Language

In Montreal or Quebec—Dates and place or places to be announced September 1st.

Revision Courses are announced as follows:—

In the subjects of the Primary Examination:

1. Toronto—Departments of Anatomy and Physiology;
apply, Miss M. Cory, Department of Physiology, University of Toronto.
2. Montreal — Departments of Anatomy and Physiology, McGill University; apply, Dr. S. Dworkin, Department of Physiology.

In the subjects of the Final Examinations:

1. Medicine and Pathology: Drs. W. de M. Seriver, J. B. Ross, W. H. Chase; apply, Dr. Seriver, 1374 Sherbrooke Street West, Montreal.
2. Surgery and Pathology:
Montreal—Dr. R. R. Fitzgerald, 1414 Drummond Street, Montreal.
Toronto—Dr. F. G. Kergin, 235 Medical Arts Building, Toronto.

The Annual Meeting of the College will be held in Ottawa on October 29th.

Candidates who are graduates of 1930 or prior thereto of a Medical School or University approved by Council shall not be required to take the Primary Examination, but shall in the Final Examination demonstrate a general and practical knowledge of the clinical application of Anatomy and Physiology.

This special examination shall be conducted by clinicians.

The privilege of this subsection of the Bylaws shall become obsolete on December 1st, 1940.

Address all communications to:

Warren S. Lyman, M.D., F.R.C.P.(C.)

Honorary Secretary,

292 Somerset Street West

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Further details will appear in
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FRACTURES AND TRAUMATIC SURGERY—Informal Course every week; Intensive Formal Course starting October 3rd.

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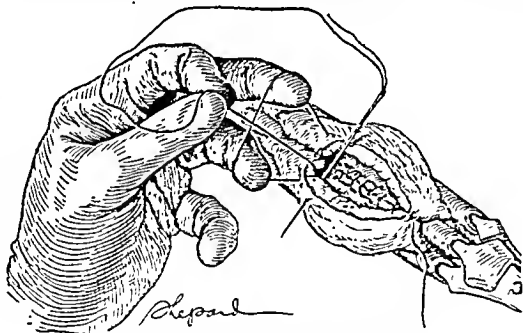
Intensive course in malignant tumors. One week, October 24-28, 1938. Lectures, operative and non-operative clinics, and demonstrations.

Seminar in traumatic surgery. One week, October 10-15, 1938. Diagnosis and treatment of fractures, and the care of damaged soft structures. Lectures, operative and non-operative clinics, ward rounds, and surgical anatomy.

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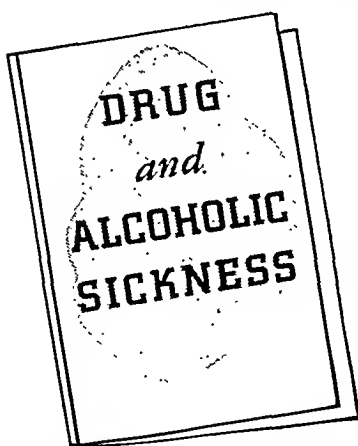
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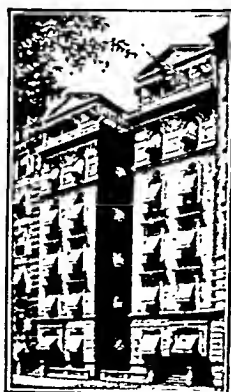
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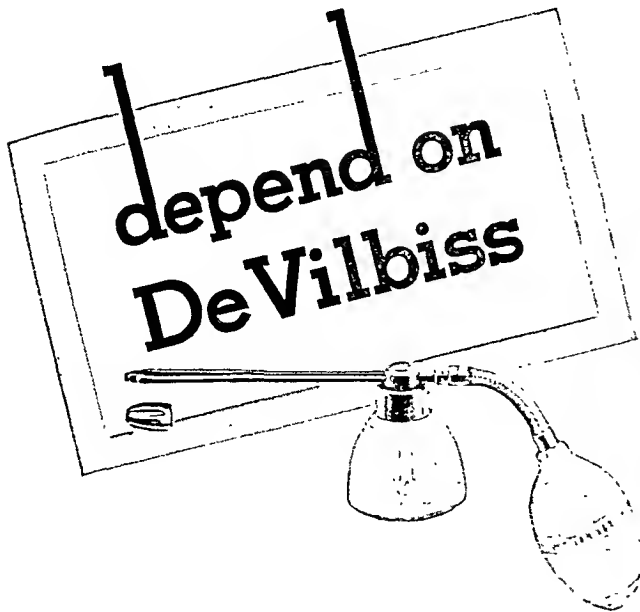
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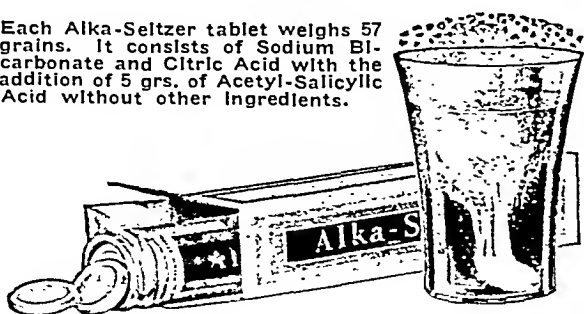
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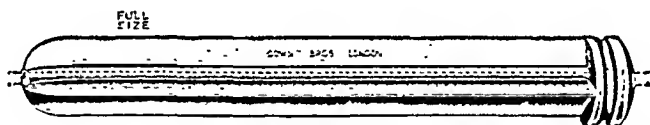
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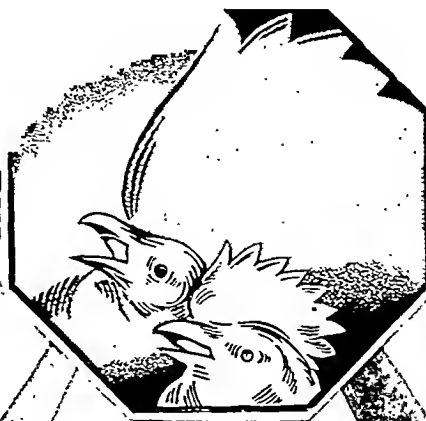
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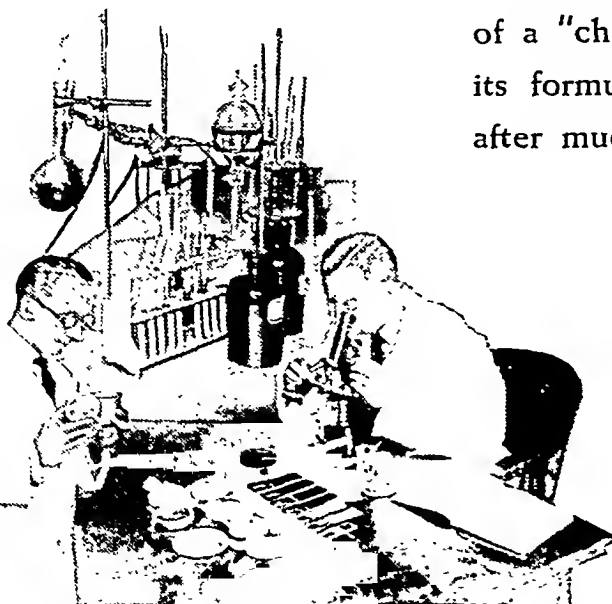
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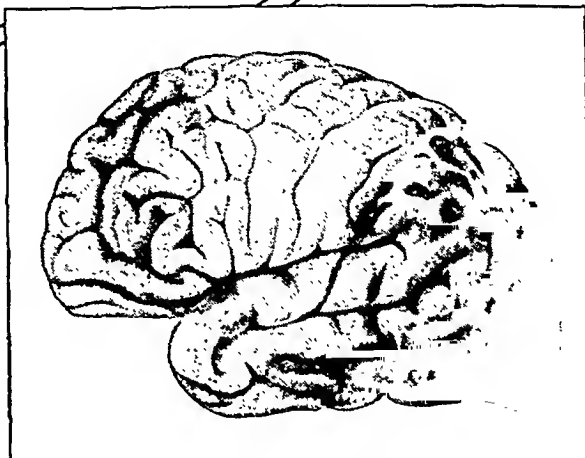
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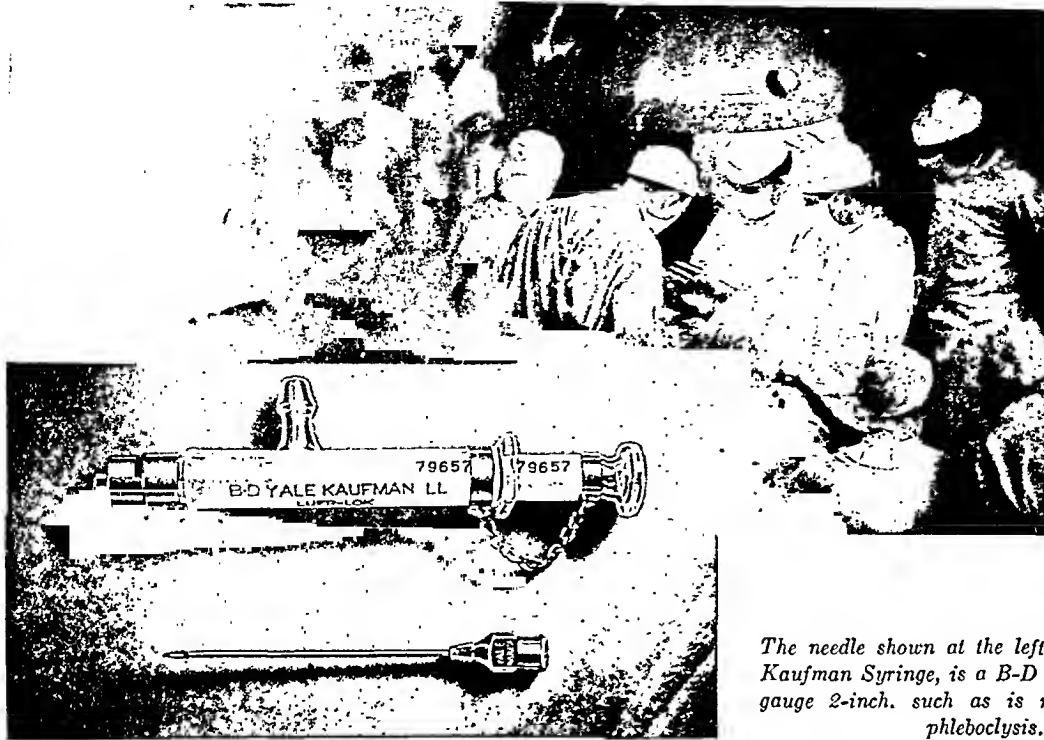
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THE B-D Kaufman Syringe—made either with a regular Luer slip tip, or with the B-D Luer-Lok tip as illustrated—has found a remarkably wide field of usefulness. Used with

a B-D 300 cc. Gravity Tube, a Glass Observation Tube, and B-D Rubber Tubing (Outfit No. K606/0), it is standard equipment with many surgeons for following operations:

INJECTION OF SALVARSAN BY GRAVITY Needle, 20 gauge $\frac{5}{8}$ ".
CONTINUOUS PHEBOCLYSIS (*venoclysis*) Needles, B-D Titus, B-D Horsley or B-D Lindeman, 16 gauge.
BLOOD TRANSFUSION (*indirect*) Needles, B-D Unger 13-18 gauge $1\frac{5}{8}$ ", B-D Lewisohn 13-18 gauge $2\frac{1}{8}$ ", B-D Kaliski 13 gauge 2" and also 15 and 18 gauge $1\frac{1}{8}$ ", B-D Fordyce 13-17 gauge $1\frac{1}{2}$ ", and B-D Lindeman 14 and 15 gauge $2\frac{1}{4}$ ", 16 and 18 gauge $1\frac{5}{16}$ ".
INTRAVENOUS CHOLECYSTOGRAPHY Needle, 19 gauge 2".

In all these operations and in others of similar character, the B-D Kaufman Syringe gives perfect control of the injection. No air can

enter the vein, for the circuit is always closed whether the plunger is *in*—to interrupt the flow, or *out*—to permit passage of the solution.

B-D PRODUCTS

Made for the Profession

B-D Products are sold through your local dealer
NORMAN S. WRIGHT & CO. LTD., TORONTO, CANADA
 Canadian Sales Representative for
BEGON, DICKINSON & CO.

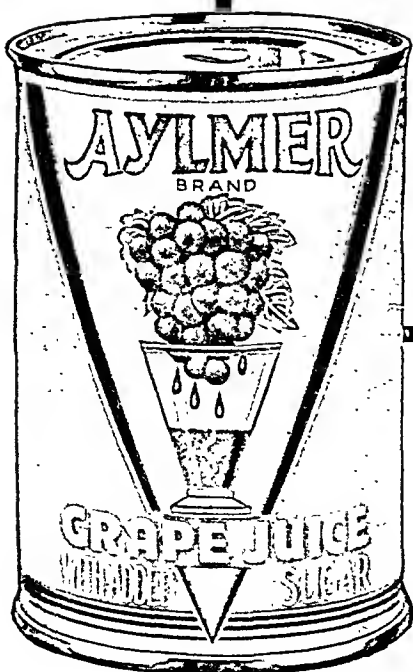
AYLMER GRAPE JUICE AS A VEHICLE

AYLMER Grape Juice is the pure juice of fully ripened Canadian Concord Grapes grown in the famous Niagara Fruit Belt. The only added ingredient is sufficient sugar to bring total sugar content up to about 17%. AYLMEER Grape Juice embodies the full flavour of the grape and will be well tolerated by the patient.

In the administration of dilute Hydrochloric Acid to Pernicious Anemia and other patients, AYLMEER Grape Juice will be found to be an excellent vehicle.

Lugol's solution can be efficiently masked in AYLMEER Grape Juice for the Thyroid case which requires Lugol's solution for treatment or maintenance.

AYLMER Grape Juice comes in handy 10½ ounce tins and the cost to the patient will be found to be very reasonable. AYLMEER Grape Juice can be safely specified for those patients who are required to take either dilute Hydrochloric Acid or Lugol's solution.



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HAMILTON **CANADA**

